Microdosimetry in Hadrontherapy

THEORY: stochastic physical quantities

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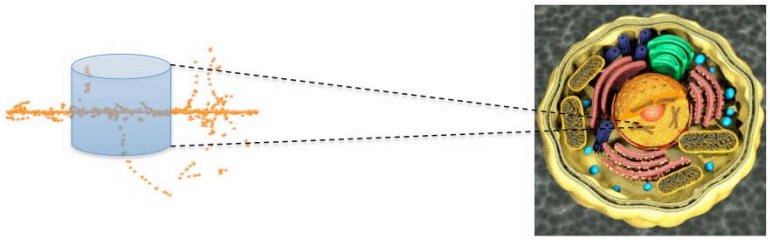
MICRODOSIMETRY

Microdosimetry is a spectroscopic technique, which stems from nuclear physics. It aims to measure the energy spectrum of events occurring in the sensitive volume of a detector when single ionizing particles hit the detector itself.



If the detector sensitive-volume material is tissue-equivalent, and its size is significant for a living cell, the microdosimetric spectrum can be used to infer the initial radiation effect on a living cell.

SOME QUESTIONS AND ANSWERS

Microdosimetry, why?

Because dosimetry fails to monitor the bio-dose of mixed-radiation filds. Biological effects of 1 Gy of gamma rays, 1 Gy of protons, 1 Gy of fast neutrons, 1 Gy of carbon ions are different.

Why does dosimetry fails?

Because the dosimetric measurement is not related to the initial damage to a living cell.

What bio-dose is related to?

Bio-dose is related to the energy imparted by a single particle to the microscopic volume containing the biological structure, which is "critical" for the cell life.

People image that nuclear radiation are like the light coming from the sun, only much stronger and penetrating. Therefore, similarly to the sun light, they think that the radiation intensity and the time exposition (namely the absorbed dose) are enough to quantify the radiation effects. But this image is not realistic.
Nuclear radiations are like a rose of hunting bullets, with more or less scattered buckshot. The bullets dose is not enough to describe the effect on the living target. The bullets calibre plays a fundamental role for the animal surviving.

SOME QUESTIONS AND ANSWERS

Why bio-dose is related to a single particle interaction?

Because the biological system reacts to the primary radiation damage, induced by a single particle, which finishes in 10^{-8} seconds. Unlikely, more than 1 particle crosses the critical biological structure in 10^{-8} seconds. More than 10^{16} particles per cm^2 per second are necessary, so that a second particle crosses the target (e.g. chromosome).

How big is the "critical" biological structure (critical site)?

We do not know really. However, it has to have a size between about 10 micrometers (human cell) and 2 nanometrs (DNA helix).

For a human cell (10 µm) 10^{14} particle/cm2·s are necessary to have, on average, more than 1 particle before the end of the physical-chemical stage.

SOME QUESTIONS AND ANSWERS

Is it possible to measure the energy imparted by a single particle to a critical site?

Yes, it is. Microdosimetry measures the energy imparted by a single particle in sites of 0.025 - 10 micrometers.

Is microdosimetry useful in radiation therapy?

It is useful everywhere the bio-dose does not scale with the absorbed dose. That happens, for instance in the radiation therapy with ions and with neutrons. It is also useful to assess the patient cancer risk due to the therapeutic treatment with radiations.

Microdosimetry is necessary to monitor the radiation quality (the relative biological effect) of mixed-radiation fields.

MICRODOSIMETRY: THEORY, DETECTORS, DATA PROCESING

THEORY

1. Microdosimetric operative quantities.
2. Microdosimetric quantity distributions.
3. The bridge microdosimetry to dosimetry.

MICRODOSIMETRIC DETECTORS

1. Gas and solid state microdosimeters.

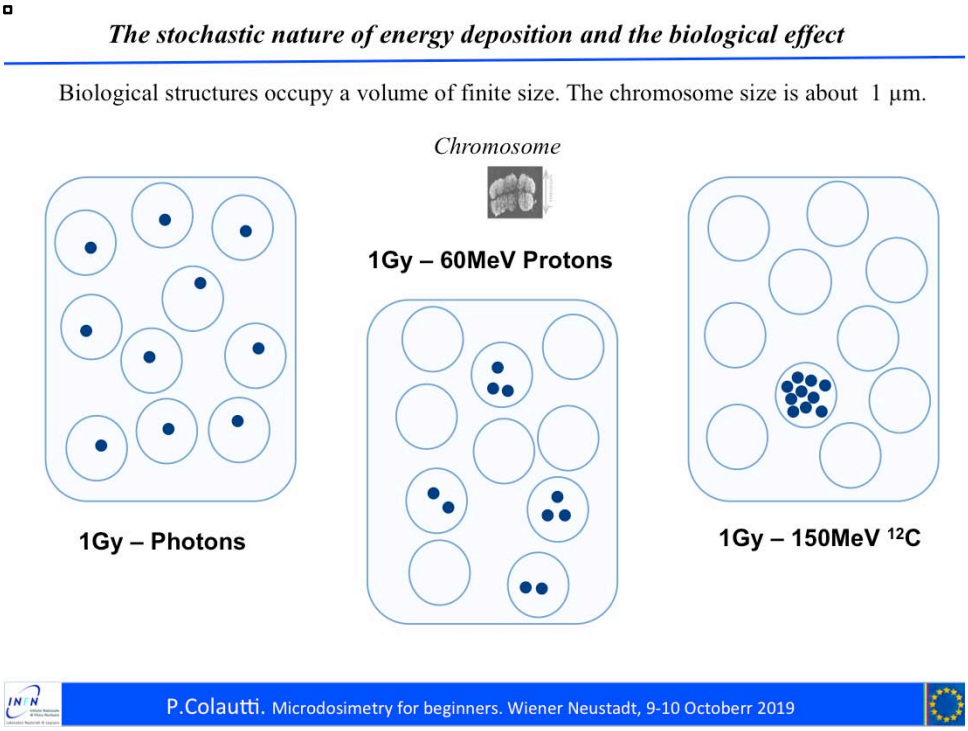
MICRODOSIMETERS AS RADIATION QUALITY MONITORS

1. Microdosimeters as LET monitors.
2. Microdosimetrs as RBE monitors.
3. Microdosimeters in mixed-radiation fields: BNCT.

MICRODOSIMETER DATA PROCESSING

1. How acquiring microdosimetric spectra that span on 4 orders of magnitude.
2. The creation of a single spectrum from 3 sub-spectra.
3. The spectrum calibration.
4. The spectrum extrapolation.
5. Exercise: to process 2 spectra (not calibrated nor extrapolated) of a proton therapeutic unit.

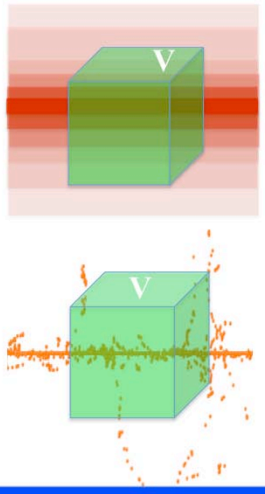
2 data.txt file will be provided to perform the exercise.



Following the hunting analogy, the same dose of bullets can be provided by small, medium or big calibre bullets. The biological effect, for the same dose of "bullets", increases with the bullet calibre.
More properly, the bullet calibre is called "imparted energy" to one of the small spherical volumes in which the target is divided in the figure.

The energy imparted, ε and ε_1 to the volume V: the physical base of the biological effect

Microdosimetry deals with the energy imparted to the volume *V* by a single, directly or indirectly, ionizing particle or by multiple particles, which cross the volume *V*.

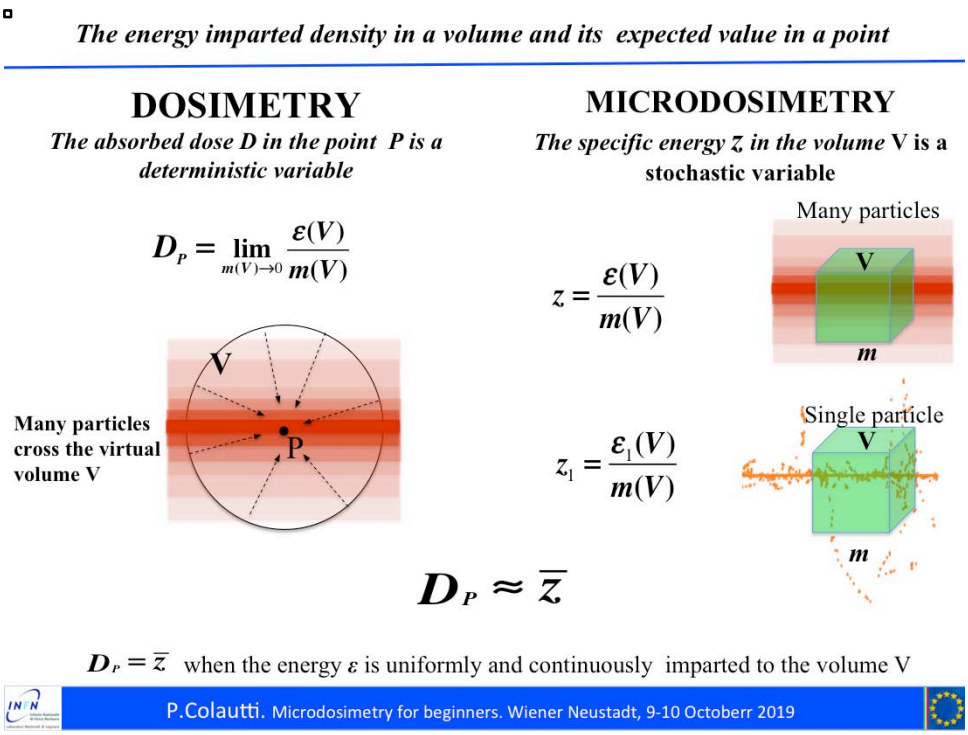


Multiple particles $\varepsilon = T_{in}^{all} - T_{out}^{all} + Q_{\Delta m}^{all}$

T is the kinetic energy.
Q is the mass-energy difference of parent and daughter nuclides in a nuclear reaction.

Single particle $\varepsilon_1 = T_{in} - T_{out}^{all} + Q_{\Delta m}^{all}$

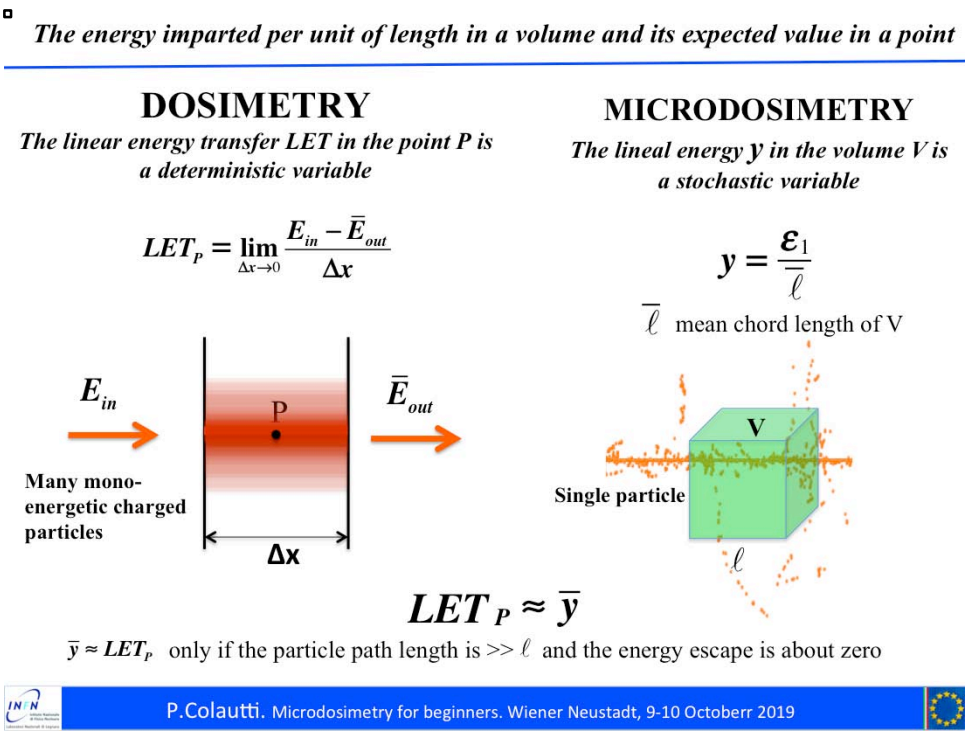
The energy imparted is simply the difference between the energy entering into the volume and the energy outgoing from the volume. If nuclear reaction occur inside the volume, part of the incoming particle+nucleus mass can be transformed in energy (e.g. neutron absorption) that energy has to be added (Q-value positive). On the contrary if part of the kinetic energy of the incoming particle is spent just to make the nuclear reaction possible, that energy has to be subtracted (Q-value negative).



There are two ways of describing the energy-imparted density in a target: in a point ***P*** or in a volume ***V***.

1. The energy imparted (here called ***œ***) in a point ***P*** is always 0. However, the lim➔0 of the ratio ***œ/m*** can be different than 0. The lim➔0 operator operates on continuous functions. Therefore, ***œ*** has to decrease uniformly with ***m*** decrease. Such picture hold only if a very large number of particles cross the mass ***m*** for any value of ***m*** and they are imaged to slow down continuously (CSDA approximation). In that conceptual frame, the energy-imparted density in the point ***P*** acquire a single value, called the dose in ***P***, namely $D_{p.}$. The subscript P is used only here for sake of clarity.
2. The energy-imparted density ***œ/m*** in a volume ***V*** can acquire many different values from particle to particle, because the indetermination dominates the collision physics at atomic and nuclear level. The ***œ/m*** fluctuation size decreases by increasing the number of particles crossing ***V***, but it never becomes 0.

Therefore, we have two sets of physical concepts, which we can



Similarly to the energy-imparted density, there are two ways of describing the energy-imparted **linear** density in a target: in a point ***P*** or in a volume ***V***.

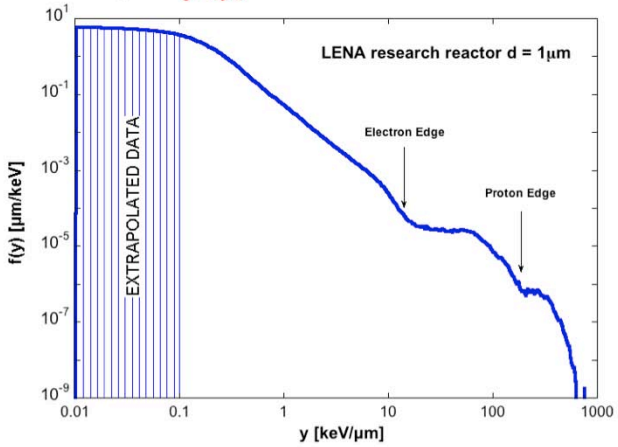
1. The energy imparted ***œ*** in a point ***P*** by charged particles of a given charge and velocity is always 0. However, the lim➔0 of the ratio ***œ/ Δx*** can be different than 0. The lim➔0 operator operates on continuous functions. Therefore, ***œ*** has to decrease uniformly with ***Δx*** decrease. Such picture hold only if the particles are imagined to cross the mass thickness ***Δx*** slowing down continuously and without loosing energy outside the track line (CSDA approximation). In that conceptual frame, the energy-imparted linear density in the point ***P*** acquire a single value, called linear energy transfer in ***P***, namely $\boldsymbol{LET_{p.}}$. The subscript P is used only here for sake of clarity.

2. In a volume ***V*** where particles can arrive from any direction, the ratio of the energy-imparted ***œ*** to the ***V*** on its mean chord length (here called ***L***), namely ***œ/L***, is called **lineal energy y** of the single charged particle in the volume ***V***. ***y*** can acquire many different values

The frequency-distribution of y and z_1 in 1 µm site of the LENA reactor neutron field

All the possible **y-values**, of a given radiation field and in a given volume, are described by the frequency distribution of ***y***. ***f(y)*** is the probability that an event in ***V*** has lineal energy ***y***. ***f(z_1)*** has the same shape of ***f(y)***, but different values in order to fulfil the normalization to 1 of the distribution.

The frequency-distribution of y is $f(y)$ The frequency-distribution of z_1 is $f(z_1)$



Note that the frequency distribution is actually a density distribution, since it is not dimensionless, but its physical dimension is the inverse of the stochastic variable dimension: 1/(keV/µm) for ***y*** and 1/Gy for z_1

Because the energy imparted in the volume ***V*** depends also on the particle track length inside ***V***, which varies from 0 to the maximum, the frequency distribution does not show sharps peaks that can be use for energy calibration in the microdosimetric measurements.

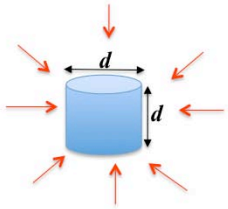
However, rapid falls of counts, called edges, can be sometime noted.
Electron edge: the fall is positioned near the maximum ***œ***-value due to one electron in ***V*** .
Proton edge: the fall is positioned near the maximum ***œ***-value due to one proton in ***V*** .

The edges can be used for energy calibration in microdosimetric measurements.

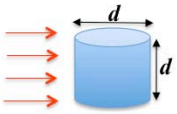
Relation between y and z_1

Being: $y = \frac{\varepsilon_1}{\bar{\ell}}$ $z_1 = \frac{\varepsilon_1}{m}$ Then $z_1 \propto y/d^2$

d: volume thickness in ***μm*** for material density of $1 g \cdot cm^{-3}$, ***y***: lineal energy in ***keV/μm***. z_1 in ***Gray***.



$z_1 = 0.136 \cdot y/d^2$ $\bar{\ell} = \frac{2}{3} \cdot d$



$z_1 = 0.16 \cdot y/d^2$ $\bar{\ell} = \frac{\pi}{4} \cdot d$

The mass density and the linear density of ***æ*** in ***V*** are not independent stochastic variables. The relating algorithm depends on the volume shape, size and density.

For cylindrical volumes, the constant in the relating algorithm depend also on the radiation field directionality, which contributes to define the mean chord length ***L***.

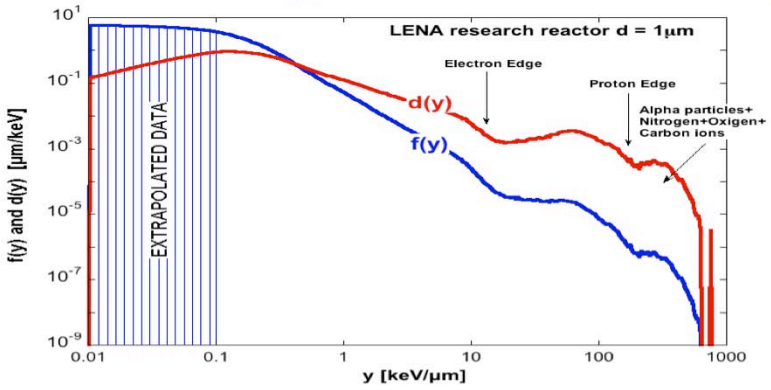
NOTE. The specific energy is proportional to the lineal energy, but the constant of proportionality includes the the inverse of the square of ***V*** diametre. For the same lineal energy (~ same LET) the specific energy (the microscopic dose in ***V***) increases rapidly with the ***V*** decrease. This finding simply explain why the absorbed dose can not assess the initial biological damage.

The dose-distribution of of y and z_1 in 1 µm site of the LENA reactor neutron field

The dose-distribution of ***y*** is the relative contribution to the dose of an event with y-value ***y*** . ***d(z_1)*** has the same shape of ***d(y)***, but different values in order to fulfil the normalization to 1.

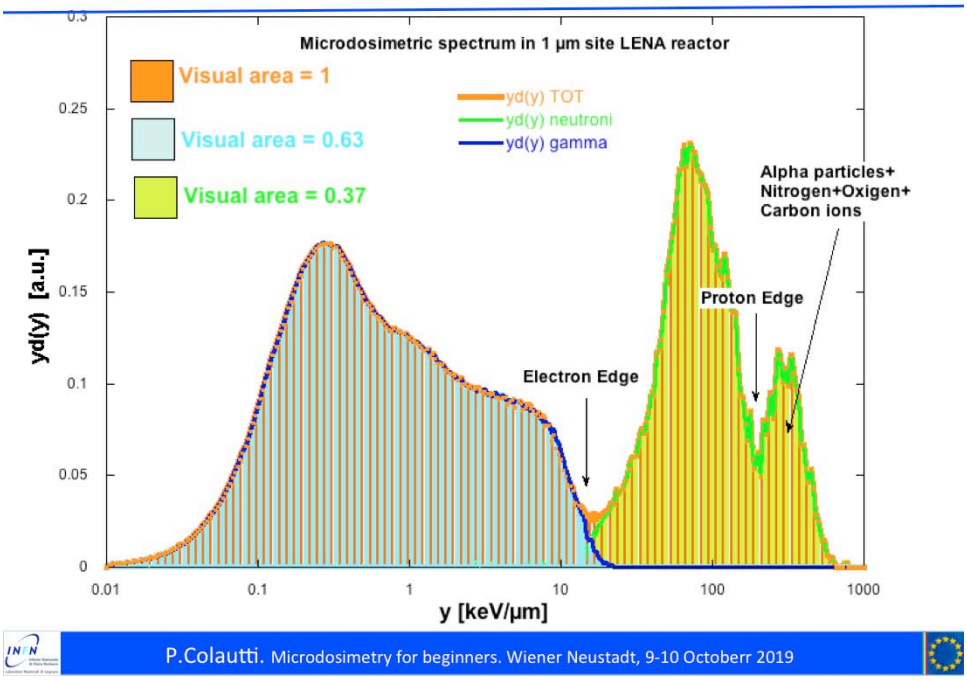
$$d(y) = \frac{y \cdot f(y)}{\bar{y}_F}$$

The dose-distribution of y: $d(y)$ The dose- distribution of z_1: $d(z_1)$



NOT all the ***œ*** value increase the dose equally. The relative increase of the dose due to events of size ***œ*** is the product of ***œ*** by the relative number of events of this size, namely ***œ·f(œ***). Therefore, the relative DOSE INCREASE, due to events of ***y*** size, is ***y·f(y)*** . Dividing the product by the normalisation factor, we obtain the probability distribution of the dose. FREQUENCY DISTRIBUTION ➔ DOSE DISTRIBUTION. The dose distribution is obtained from the measured frequency distribution.

The "visual" dose-distribution of of y in 1 µm site of the LENA reactor neutron field



Because of the large range of ***œ*** values as well of the large range of ***œ*** frequency occurrence, f(y) and d(y) have to be shown in double logarithmic plots, which are not of easy lecture. Therefore, the usual representation of the dose distribution of ***y*** is to plot ***y·d(y)*** against ***y*** in a semi-log plot. In such a representation the relative contributions to the absorbed dose of different ***œ*** events can be deduced (qualitatively) at glance without necessity of calculations.

The expectation values, or mean values, of the probability distributions

The frequency-mean of y is the mean value of y. The dose-mean of y is the y-value mean contribution to the dose. Similarly for z_1.

The **frequency-mean** of y

$$\bar{y}_F = \int_0^{y\max} y \cdot f(y) \cdot dy$$

The **frequency-mean** of z_1

$$\bar{z}_{1F} = \int_0^{z_1\max} z_1 \cdot f(z_1) \cdot dz_1$$

The **dose-mean** of y

$$\bar{y}_D = \int_0^{y\max} y \cdot d(y) \cdot dy$$

The **dose-mean** of z_1

$$\bar{z}_{1D} = \int_0^{z_1\max} z_1 \cdot d(z_1) \cdot dz_1$$

The average values of the distributions are handled easier than the distributions, although they represent a strong simplification of the interaction.

The single-particle microdosimetric mean values are DETERMINISTC variable. In other words they acquire ALWAYS THE SAME VALUE (if the statistics is high, namely if the total number of events of spectra is high) in stable and steady conditions. However, they are not, neither conceptually nor numerically, equal to the DOSIMETRC quantities. In fact the mean value $\boldsymbol{Z_1}$ does not depends on the dose. Its value is always the same at any dose. Similarly the mean value ***Y*** changes with ***V*** *thickness* even if the ***LET*** value does not change.

Relationships between mean values

If the frequency spectrum of y is known, the mean values of y and z_1 can be calculated

$$\bar{y}_D = \frac{\int_0^{y\max} y^2 \cdot f(y) \cdot dy}{\bar{y}_F}$$

$$\bar{z}_{1D} = \frac{\int_0^{y\max} z_1^2 \cdot f(z_1) \cdot dz_1}{\bar{z}_{1F}}$$

where $z_1 \propto y/d^2$

The next step is to find the relationships between the two different means.
Again: the mass-density of the energy imparted to ***V*** increases strongly with the decrease of the volume diametre, also if the ***y***-value does not change.
Example: proton of 4 MeV ➔ 0.2 mm of range in tissue ➔ 1µm is crossed without loosing velocity significantly ➔ the **mean y-value** is the same when the proton crosses 1µm volume or 0.1µm volume (10 keV/µm). . HOWEVER, the mean specific energy z_{1D} (we can call it "micro-dose" in the volume ***V***) in the 0.1 µm volume is 100 time higher than that one in 1 µm volume.

Multi-event microdosimetry

It is the theoretical **bridge to pass from microdosimetry (single-event distribution of specific energy) to dosimetry**.

The absorbed dose is indeed the **mean value** of the **multi-event distribution** of specific energy .

The single-particle microdosimetric mean values are DETERMINISTC variable: in stable and steady conditions they acquire ALWAYS THE SAME VALUE (if the statistics is high, namely if the total number of events of spectra is high)
However, they are not, neither conceptually nor numerically, equal to the DOSIMETRC quantities. In fact $\boldsymbol{Z_1}$ (mean of the z_1 distribution) does not depends on the dose, its value is always the same at any dose. Similarly the ***Y*** (mean of the y distribution) value changes with ***V*** *thickness* even if the ***LET*** values does not change.

The "mathematical and conceptual bridge" from microdosimetry to dosimetry is the multi-event distribution of specific energy ***z***. Note that ***z*** is the mass-density of ***œ*** when multi particle (not a single particle) cross ***V*** .

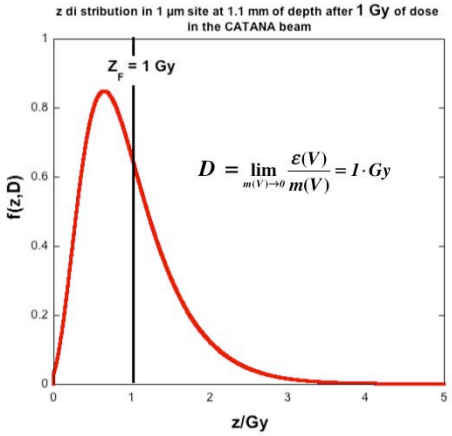
The frequency distribution of z at the dose D

The probability to have the specific energy z in V after the dose D, which has given rise to n events in V, is the sum of all the n-fold convolutions of $f(z_1)$ multiplied by the probabilities of occurrence of n events.

$$f(z;D) = \sum_0^{\infty} \frac{\left(\frac{D}{\bar{z}_{1F}}\right)^n}{n!} \cdot e^{-\frac{D}{\bar{z}_{1F}}} \cdot f_n(z)$$

Probability to have n events in V

n-fold convolution of $f(z_1)$



Also ***z*** is a stochastic variable. However, the mean value of ***z*** in the volume ***V*** is a deterministic variable. If the material density is uniform in ***V*** and if the particle fluence is uniform in ***V***, the mean value of ***z*** at the dose ***D*** is just the dose D_P, where the point ***P*** is the centre of the volume ***V***.
The microdosimetric quantity z_1 leads to ***D*** when ***V*** → ***0*** many particles cross ***V*** at any size and the interaction is continuous (CSDA approximation).

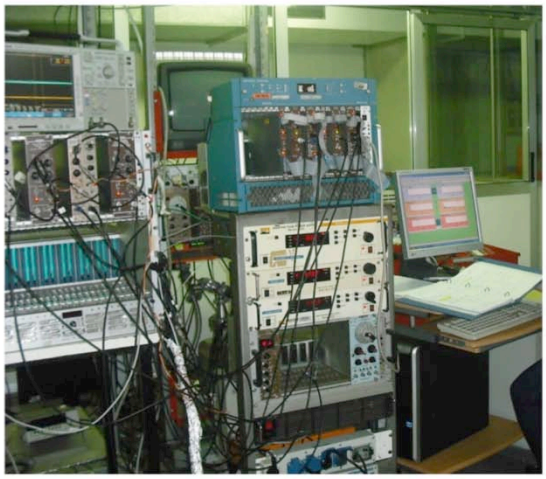
Microdosimetry in Hadrontherapy

MICRODOSIMETRIC DETECTORS: gas and solid state counters

Paolo Colautti, *INFN*

Experimental microdosimetry

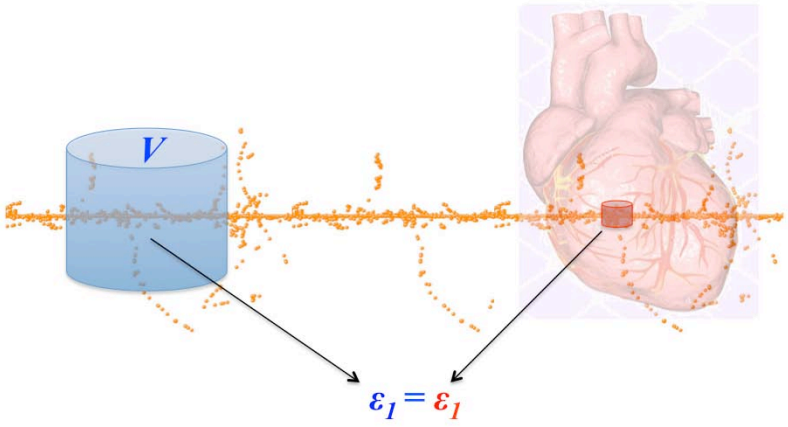
Experimental microdosimetry uses the electronic set-up of nuclear spectroscopy and special spectrometers.



Microdosimetry quantities are OPERATIVE quantities. Microdosimetry has been conceived to be an EXPERIMENTAL approach to the radiation physics. The data acquisition system is typical of nuclear spectroscopic measurements. The data acquisition system to be used in clinic can be very compact.

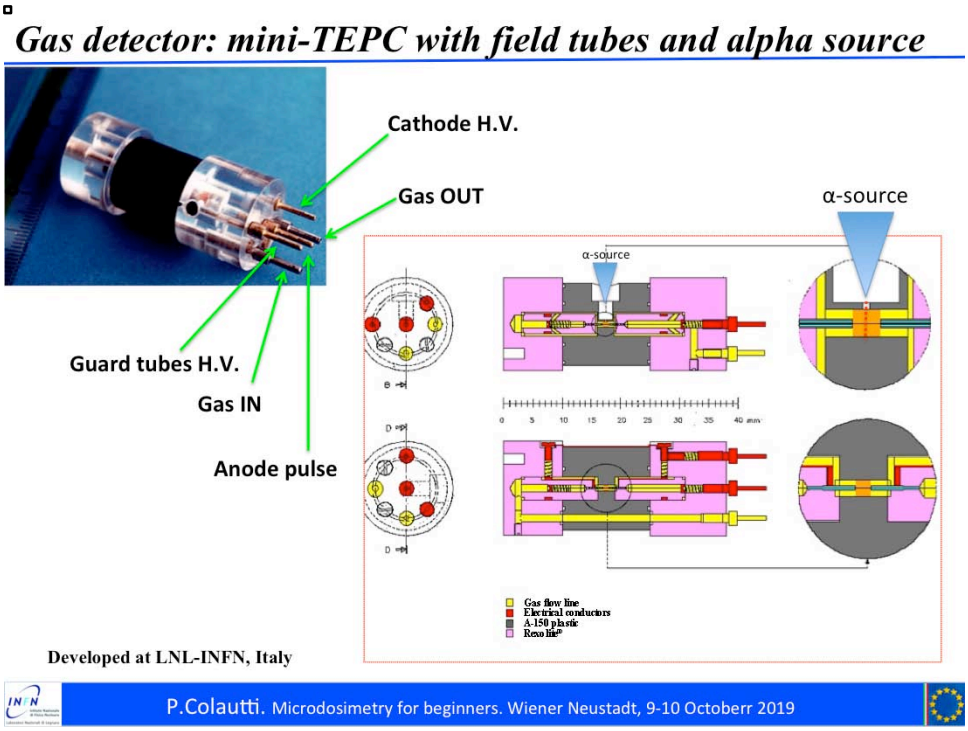
Tissue-equivalence

The imparted-energy ε_1 to the sensitive-volume V of the detector is equal to ε_1 imparted to a piece of human tissue of micrometric size.



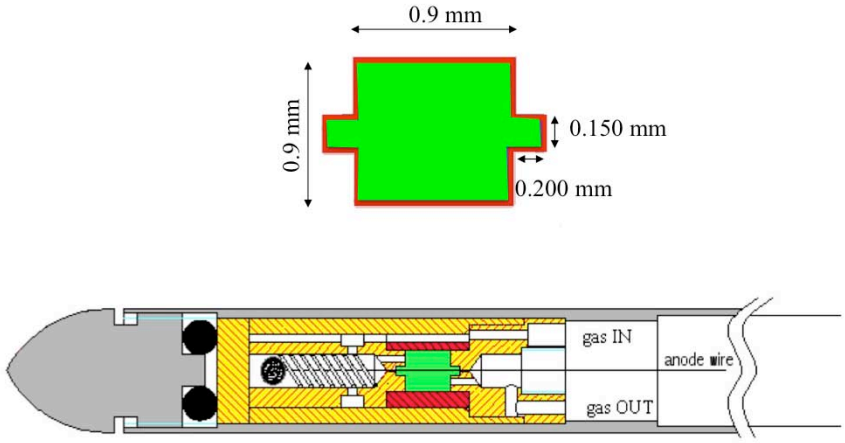
The experimental microdosimetry in radiation therapy is a model that simply states: we measure with a tissue-equivalent detector the initial damage in a piece of tissue. The tissue-equivalence is intended as imparted-energy equivalence.

The model is certainly a simplification of the interaction radiation-matter, but it is realistic, since the tissue complexity involve atomic and chemical bonds, the energy of which (eV) is much less than the imparted-energy.



A tissue-equivalent gas proportional-counter (TEPC) with a small (1mm) sensitive volume. We call it mini-TEPC. The cathode wall is thick, since it houses an alpha source.

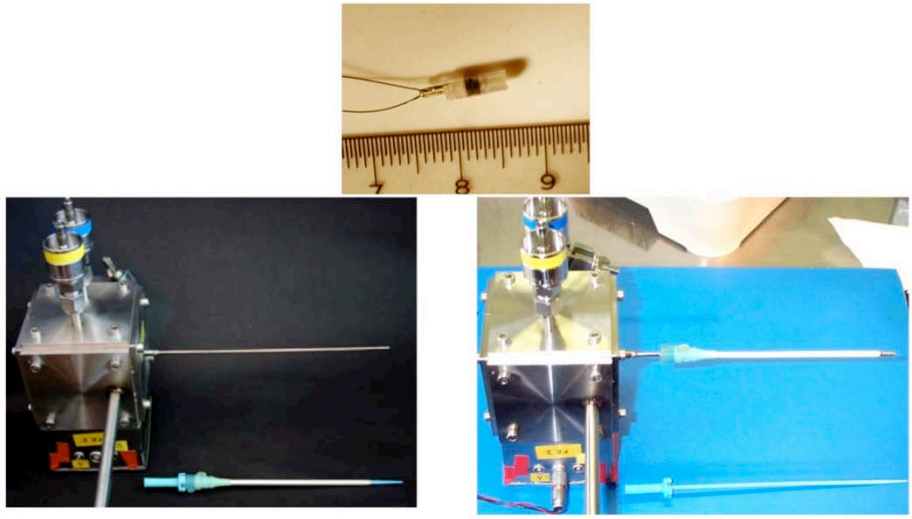
Gas detector: "naked" mini-TEPC



Developed at LNL-INFN, Italy

This mini-TEPC is "naked because it is without field tubes and calibration alpha source. Because of that, the detector encumbrance is small (2.7 mm of external diametre).

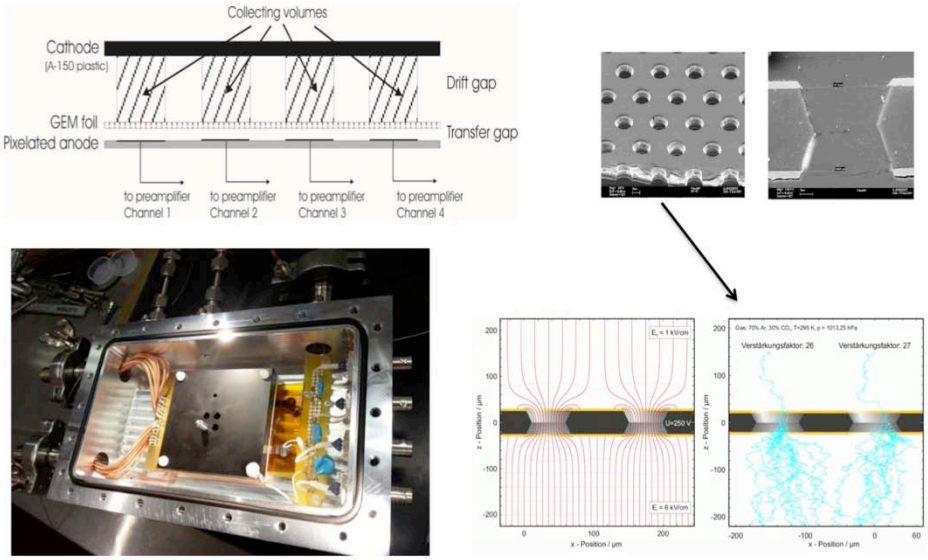
Gas detector: mini-TEPC for "in-body" measurements"



Developed at LNL-INFN, Italy

The naked mini-TEPC is inserted in a 2.7mm titanium sleeve. It can be used also for internal body measurements, with a 8 French cannula.

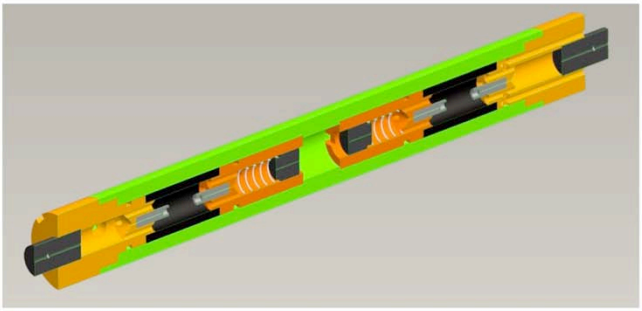
Gas detector: 2D array of mini-TEPC with GEM technology

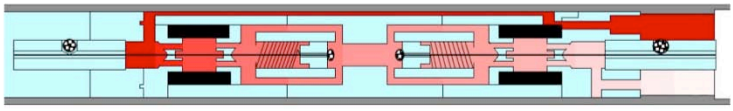


Developed at the University of Padova, Italy

2D mini-TEPC counter is an array of cylindrical TEPCs of 2 mm diameters and height. The sensitive volumes are defined by the electric field lines.

Gas detector: twin mini-TEPC for BNCT

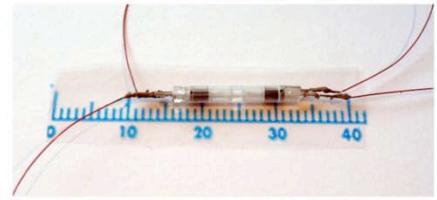


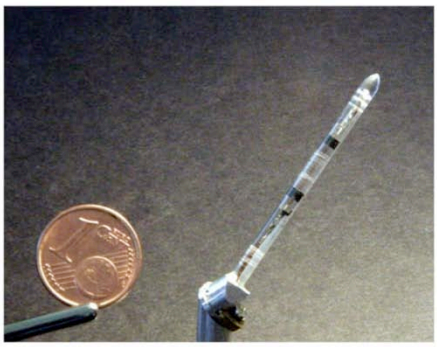


Developed at LNL-INFN, Italy

Two mini-TEPCS assembled together inside an aluminium sleeve. The cathode wall of one of them is doped with 50ppm of ^{10}B. This “twin mini-TEPC” is able to monitor the initial damage that is generated in a normal living cell and in a cell drugged with 50ppm of ^{10}B exposed to a neutron field.

Gas detector: twin mini-TEPC for BNCT

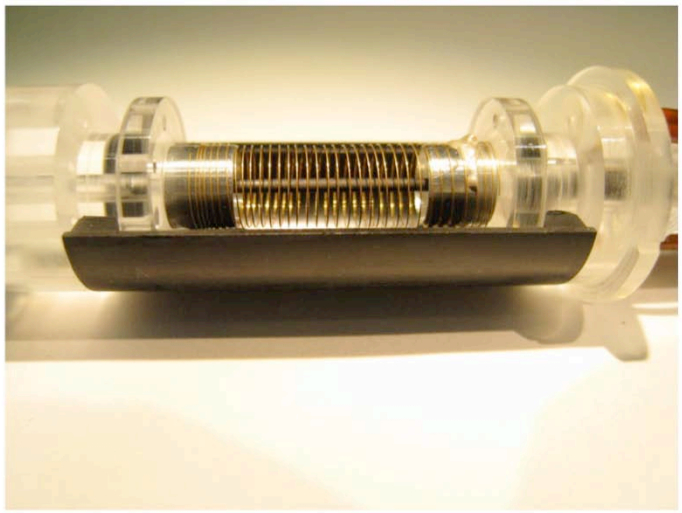




Developed at LNL-INFN, Italy

The twin mini-TEPC before being inserted inside the aluminium sleeve.

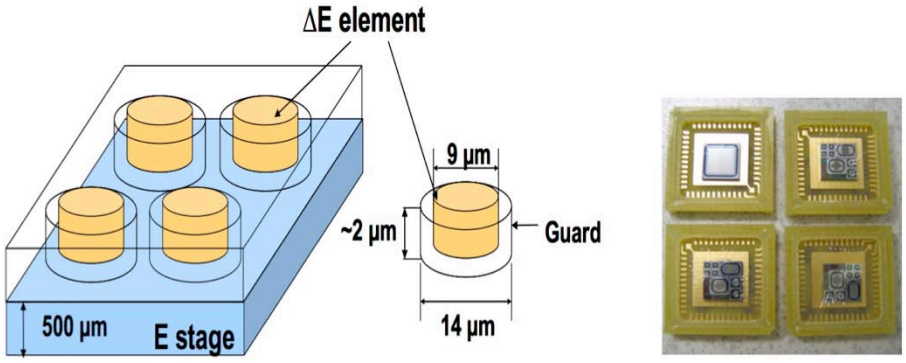
Gas detector: TEPC at avalanche confinement



Developed at LNL-INFN, Italy & Polytechnic Institute of Milano, Italy

The thick anode of this unusual gas proportional counter is surrounded by one helix, the aim of which is to confine the electronic avalanche inside itself. In such a way 80% of sensitive volume is avalanche free also at very low gas pressure. This “trick” allows to measure microdosimetric spectra in very small sensitive volumes, in order to monitor the initial damage in biological structures less than 1 µm of size (down to 0.025 µm).

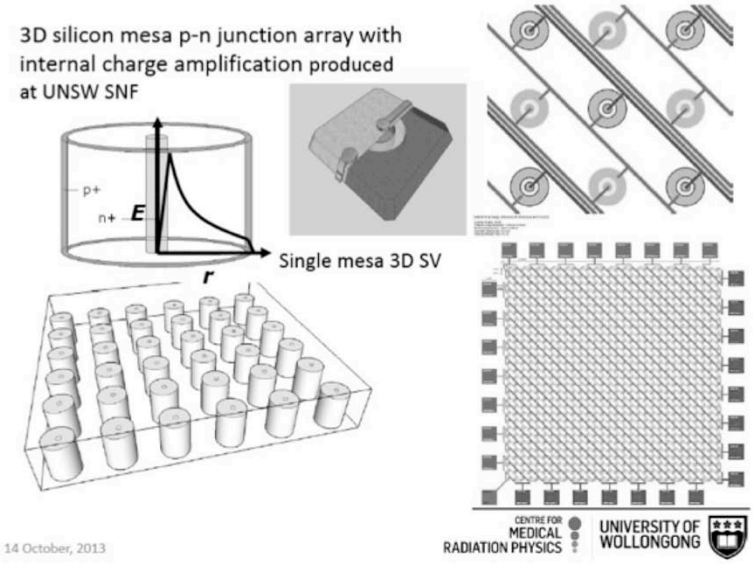
Solid state detector: the silicon telescope



Developed at Polytechnic Institute of Milano, Italy

ΔE-E detectors are used in nuclear physics to recognise charge and energy of particles hitting the detector. In microdosimetry, this feature allows to distinguish the energy imparted ***œ*** due to the different charged particles of a mixed-radiation field. This allows also to choose pulse by pulse the right factor to scale from ***œ*** in silicon to ***œ*** in tissue.

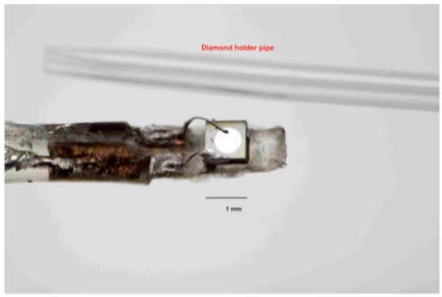
Solid state detector: the 3D silicon counter array

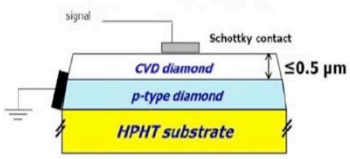


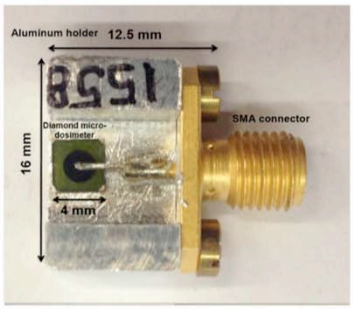
Developed at University of Wollongong, Australia

An array of cylindrical silicon microdosimeter.

Solid state detector: the diamond counter







Developed at University of Roma II, Italy & MedAustron Institute, Austria

Artificial diamond are already used to measure the dose in clinic. Recent technological advances have made it possible to manufacture very thin sensitive volume of micrometric thickness.

The main differences between gas and solid state detector

	Gas detectors	Solid state detectors
Detection efficiency	HIGH	LOW
Applied voltage	HIGH	LOW
Tissue equivalence	YES	NO
Particle fluence rate	$\leq 4 \cdot 10^6$ cm^{-2}s^{-1}	Higher
Volume equivalent size	0.025 – 2 µm	4 - 40 µm
4π response	~YES	NO

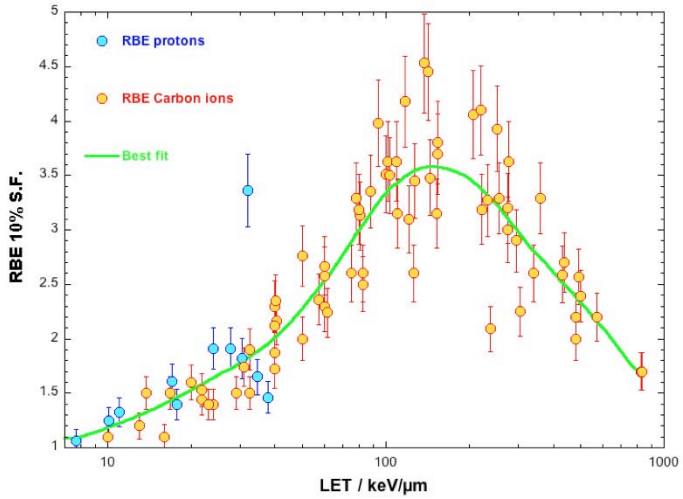
Gas detectors allow to amplify the electrical charge generated in the sensitive volume by an ionizing particle. Therefore, they can measure very small *œ* values. However, they need high voltage. Moreover, they hardly can have sensitive volumes less than 1 mm of geometrical size. On the contrary, solid state detectors can be very small. Moreover, they do not need high voltage.

Microdosimetry in Hadrontherapy

MICRODOSIMETRIC AS RADIATION QUALITY MONITORS

Paolo Colautti, *INFN*

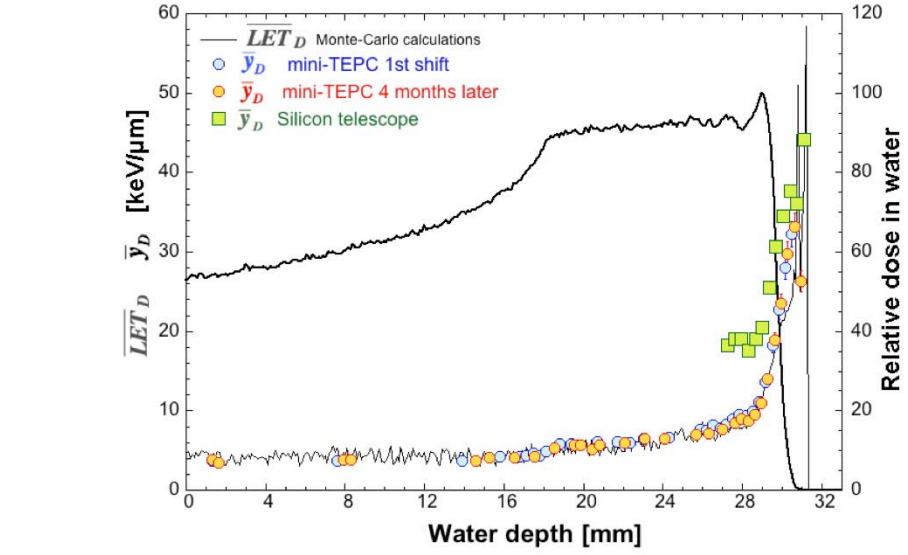
LET is often used as variable to quantify the biological effect



Although the same dose is imparted, radiobiological effects can be quantitatively different with kind and energy of the particle. A way to quantify this difference is the RBE (ratio of gamma rays dose on particle dose to obtain the same effect). RBE_{10} is the dose ratio measured at 10% of cell surviving fraction. Changing the surviving fraction, the RBE value can change. Many radiobiological experiments have correlated RBE values with LET values. Radiobiological data of a laboratory have precision of ~ 10%, but when the results of different laboratories are put together, data fluctuate much more.

One manner to quantify the "radiation field quality" is to calculate its average LET value.

Measurements at CATANA facility: dose-mean LET and $\bar{y}_D$

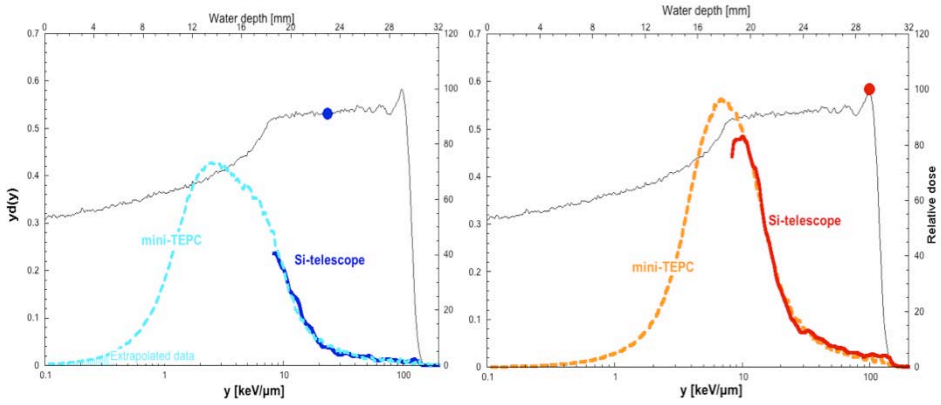


The ***dose-mean y-value*** can monitor the ***dose-mean LET*** value of a proton beam? (remember that the mean value of ***d(y)*** is not equal neither conceptually nor numerically to the dose-mean LET) Yes, mini-TEPC can do it pretty well. Silicon detector can do it only partially.

yd(y) spectra of mini-TEPC (d=1 µm) and Si-telescope (d=4.4 µm)

The microdosimetric efficiency η is the ratio: ***detected dose-events/dose-events occurring in the detector sensitive volume***

$\eta = 0.99$ $\eta = 0.16$ $\eta > 0.99$ $\eta = 0.43$

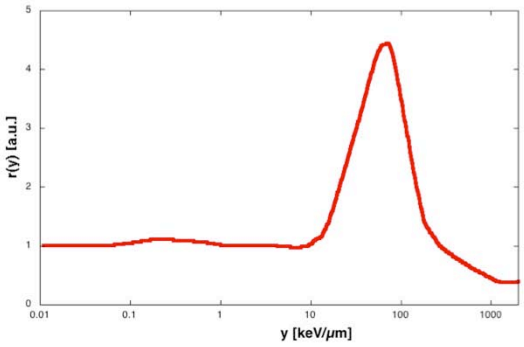


The reason of the only partial capability of silicon detectors to monitor LET is their small detection efficiency, since they are not able to measure very small ***œ*** values, because of the electronic background noise.

RBE assessment by using the d(y) spectrum

The cell response model states that for a given radiobiological end-point and for a given y-value in the critical volume ***V***, the cell response is ***r(y)***. Similarly, the relative biological effectiveness for a given y value is ***RBE(y) = r(y)·d(y)*** and for all the spectral dose:

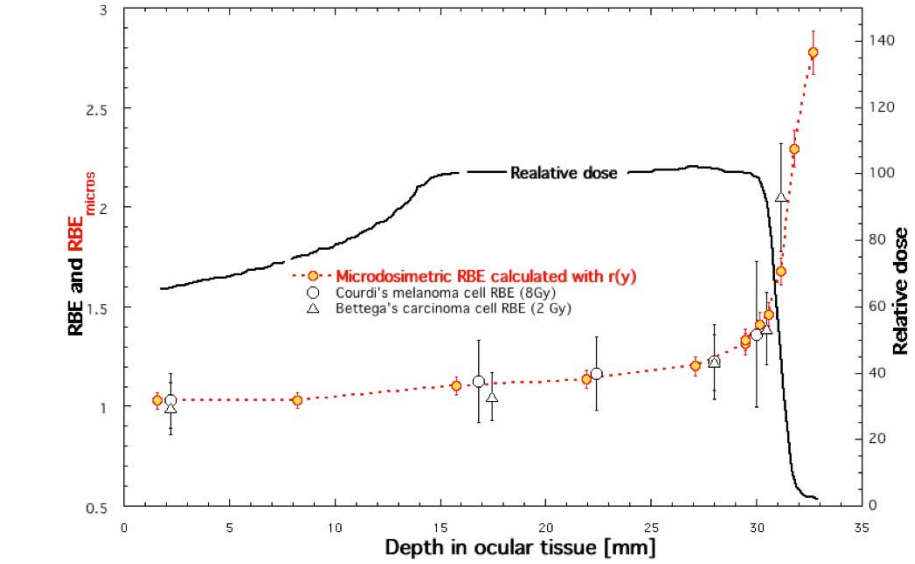
$$RBE = \int_0^{y\max} r(y)\cdot d(y)\cdot dy$$



It has been shown that the r(y) is unique for photons, fast neutrons and protons

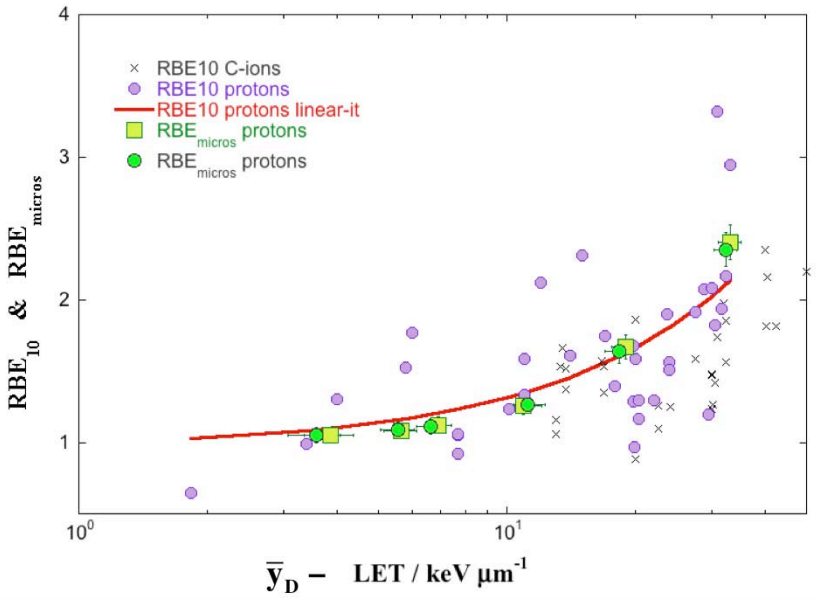
Microdosimeters can also monitor the RBE by using the response function ***r(y)***.
r(y) is the cell response to an event of size ***y***. This function can not be directly measured. However, it can be extracted by a set of integral equations where the ***radiobiological RBE*** value is equalled to the ***microdosimetric RBE*** value.

61.5 MeV Protons of the Antoine-Lacassagne Centre, Nice, France



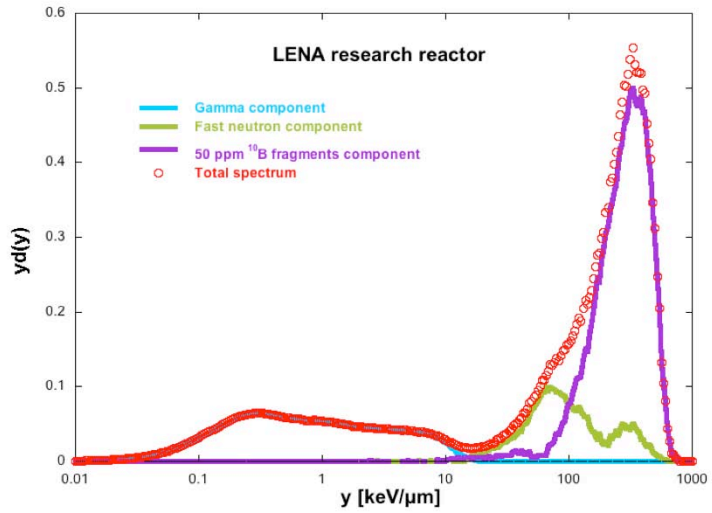
Microdosimetric RBE values (RBE_{micros}) of the therapeutic proton beam of Nice fit well the radiobiological RBE data taken in the same proton beam.

62 MeV Protons of the CATANA Centre, Catania, Italy



Similar measurements have been recently repeated at the CATANA therapeutic beam with a SEALED mini-TEPC. RBE_{micros} data superimpose well the linear best fit of literature RBE data.

Microdosimetric monitoring of the BNCT mixed radiation field

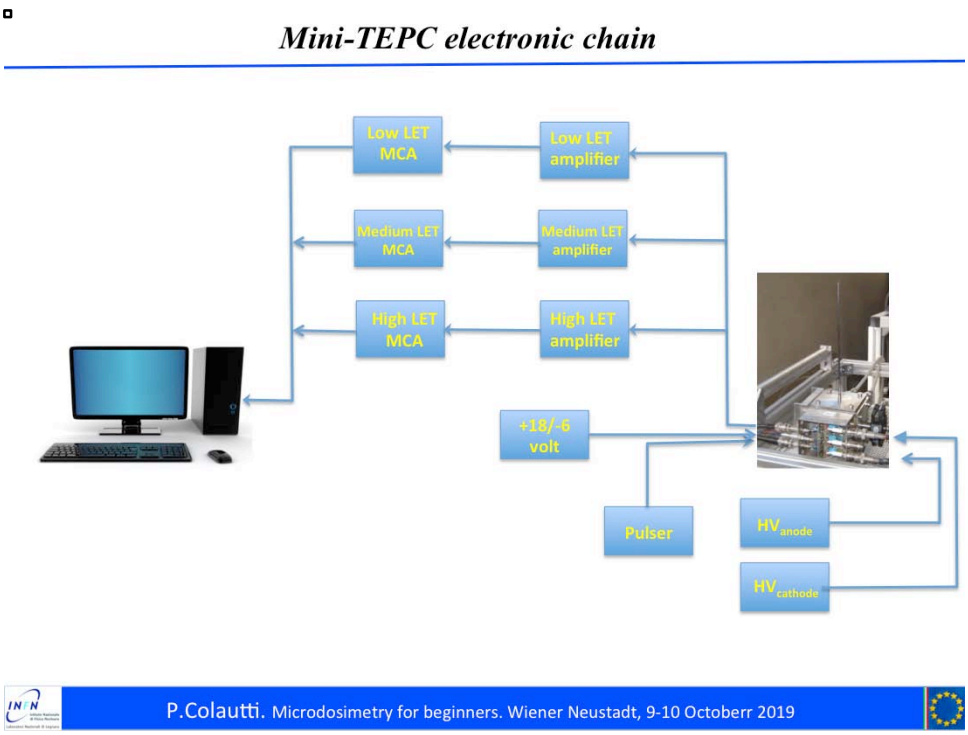


BNCT is a binary radiation therapy. The microdosimetric spectrum, taken with the twin mini-TEPC, shows the three main components of the dose. The 3 relative dose components can be measured with ~ 5% of accuracy. The microdosimetric spectrum can be used to quantify the total radiation quality as well as the quality of any radiation component.

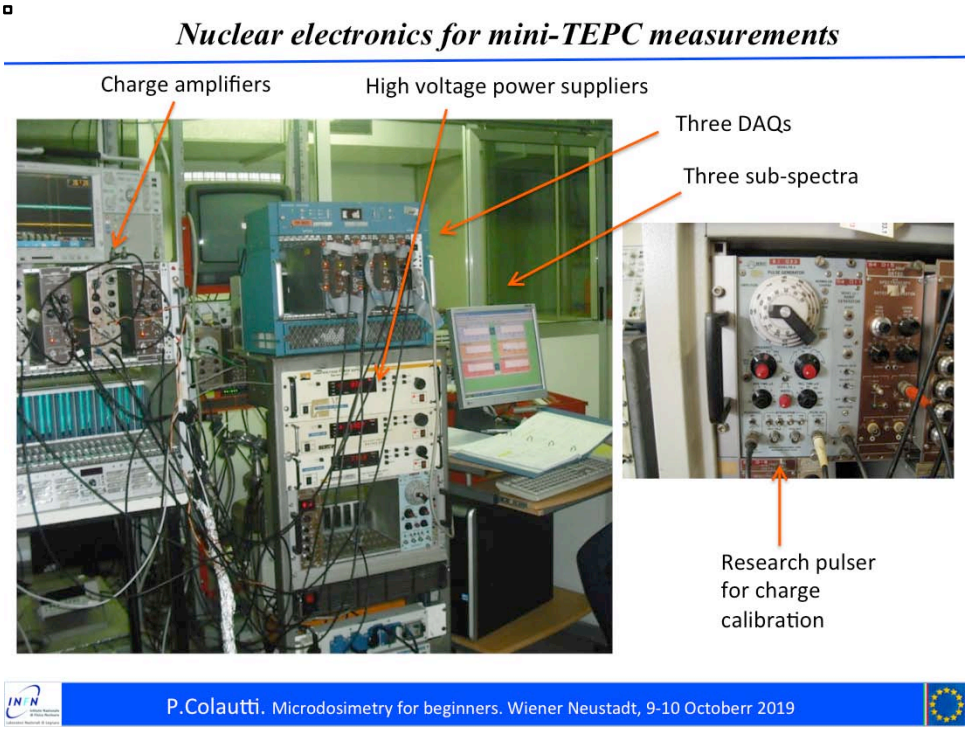
Microdosimetry in Hadrontherapy

MICRODOSIMETRS DATA PROCESSING

Paolo Colautti, *INFN*

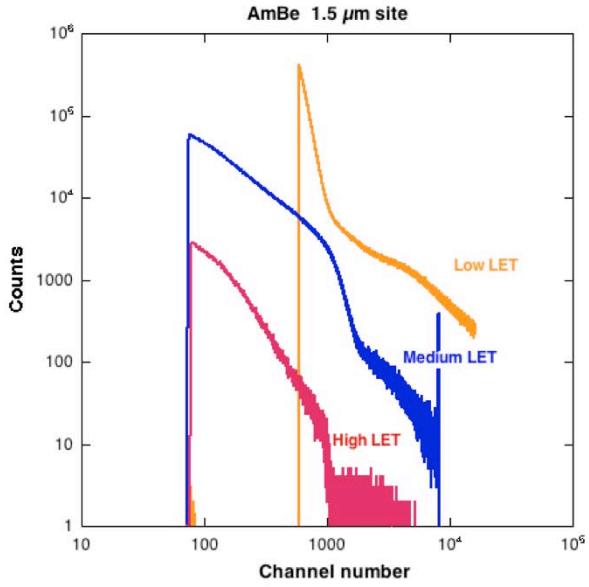


Because α values can span on more than 4 orders of magnitude, the pulse from the charge pre-amplifier, which has to have a large enough dynamic range, is differently amplified by three linear amplifiers that feed three DAQs, in order to have the same resolution both for small pulses and big pulses.



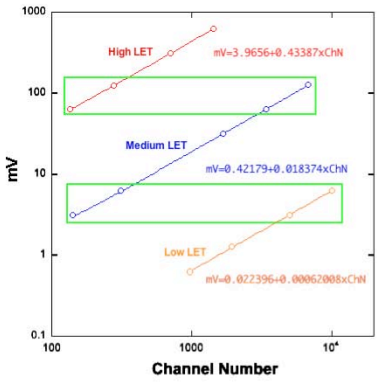
In the figure the standard acquisition system used in applied nuclear physics for spectroscopic measurements. It certainly appears rather cumbersome. However, it can be reduced to a small portable box for clinic microdosimetric applications.

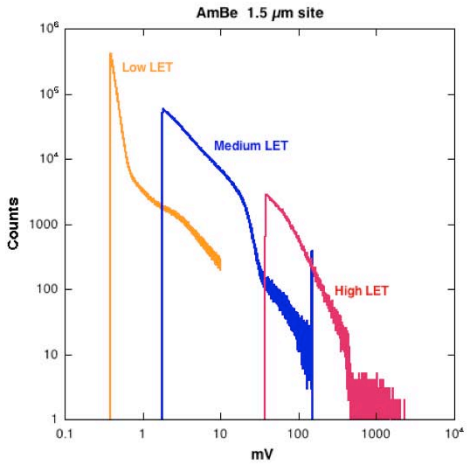
The three microdosimetric sub-spectra of an Am-Be neutron source



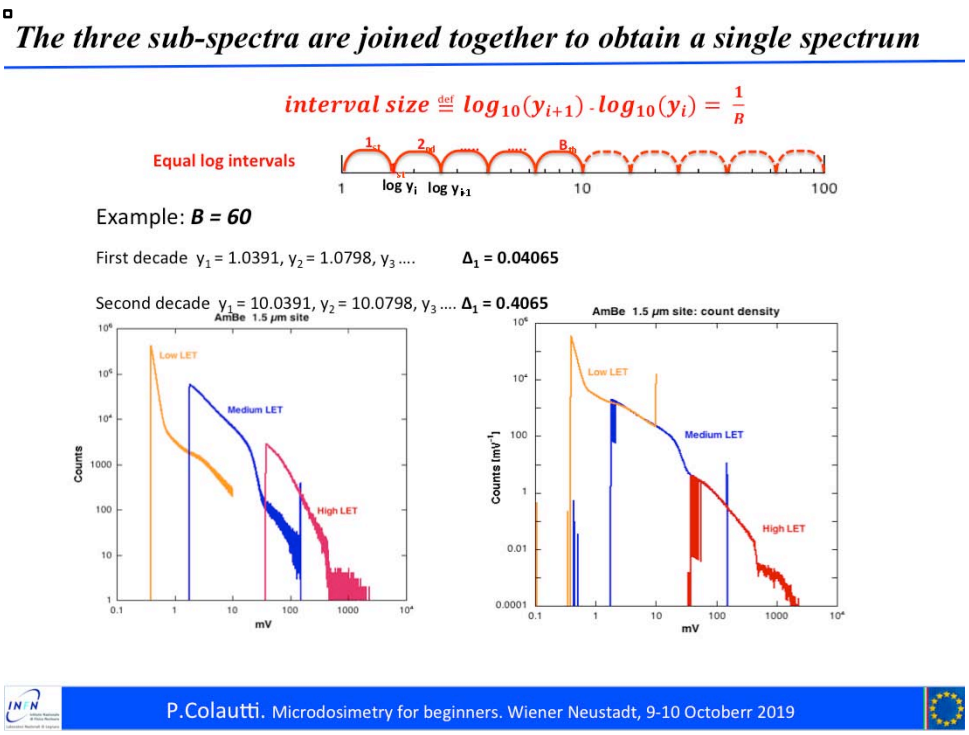
From the three linear amplifiers we obtain three sub-spectra, which are conventionally called low-LET, medium-LET and high-LET sub-spectrum.
Pay attention that the count number in ordinate is actually the numbers of counts per DAQ channel size (a count density).

The three sub-spectra after the volt calibration



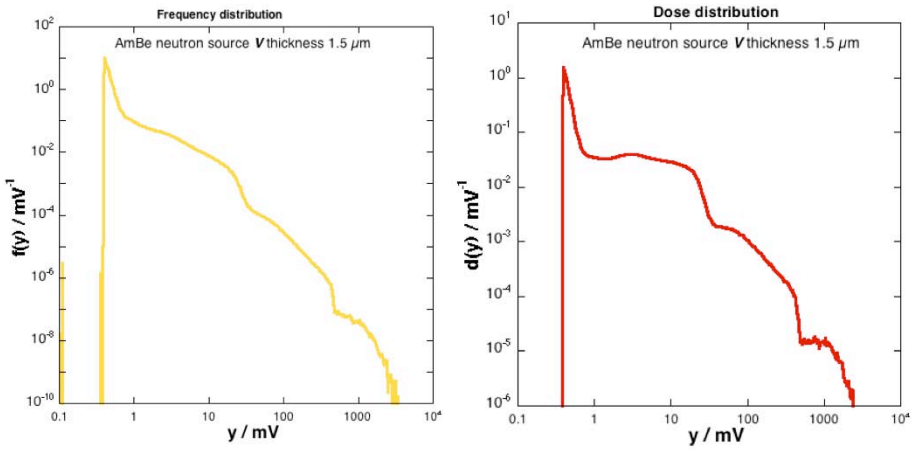


After the channel ➔ mV calibration, the DAQ's channel width becomes the voltage width ΔV. Therefore, the count number is the number of counts per ΔV of a DAQ channel size. During the amplifiers setting, attention has to be paid in order to have part of sub-spectra in the same Δœ range, that means a partial superimposition of the sub-spectra.



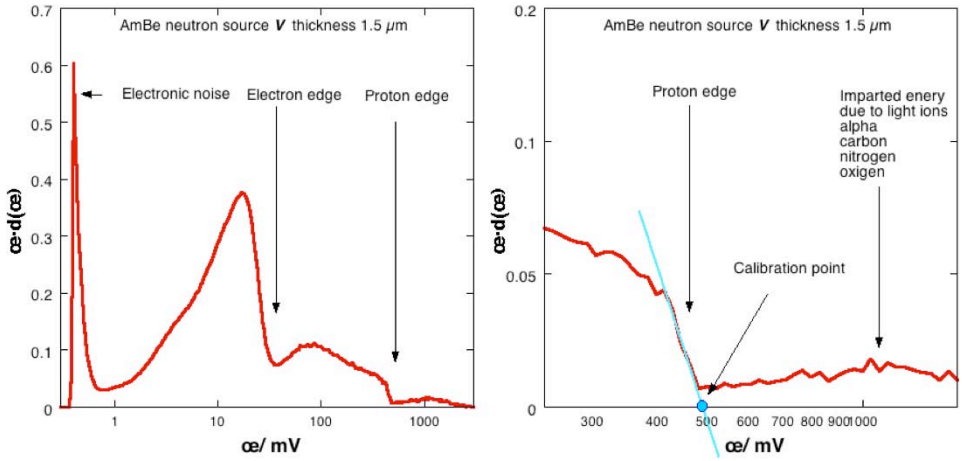
Thanks to the partial superimposition, the three sub-spectra can be vertically shifted to be joined together, in order to obtain a single spectrum with the same resolution at any ***œ***-value decade. Since the final results will be in a semi-log plot, equal resolution for small and big ***œ***-values means equal data interval, where the intervals are in logarithmic scale. In order to obtain that result, the original counts (which were acquired in a **linear** array of different ***œ***-values or ***y***-values) have to be compacted in equally spaced logarithmic intervals (in the figure the example of 60 logarithmic-equal intervals per decade).

The AmBe neutron source microdosimetric spectra (not yet calibrated)



After the joining of the tree sub-spectra, we obtain a single spectrum, which has to be normalized to obtain ***f(œ)***. Note that the physical dimension of the stochastic variable ***œ*** is now ***mV***. The product function ***f(mV)·mV*** has to be normalized again to obtain ***d(mV)***.

The calibration procedure of the microdosimetric spectrum

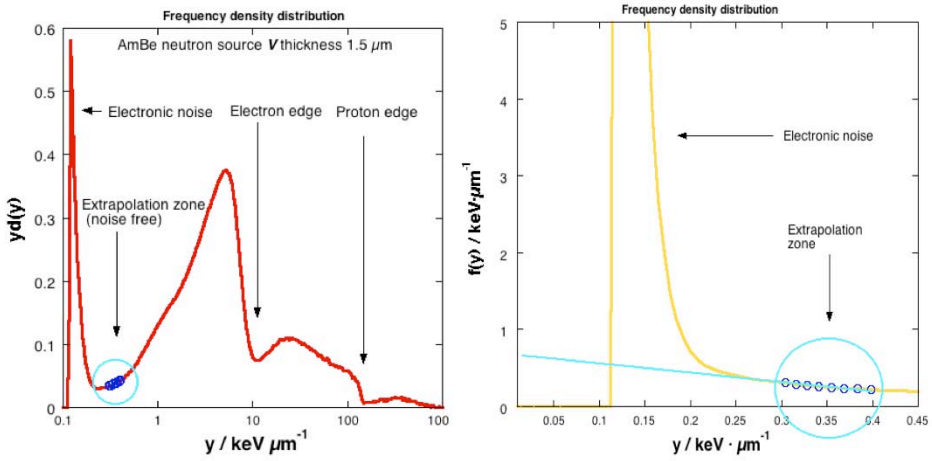


The product spectrum ***œ·d(œ)*** (expliciting the pysical dimensions: ***mV·d(mV)*** shows some clear structures. The peak at low ***œ***-values is noise. The fall at about 30 mV is the electron edge. The fall at about 500 mV is the proton edge. The last fall is used for the spectrum calibration. Pulling a straight line tangent to the fall inflection, the intercept with the ***0X*** axis gives the calibration point value (500 mV). On the other side, we know that the maximum imparted energy of a proton in a tissue site of 1.5 µm is 149 keV. Dividing that value for the mean chord length of the counter sensitive volume (1.0 µm), we obtain the lineal energy of 149 keV/µm. Therefore, multiplying the 0X axis by the ratio 149/500, we obtain the spectrum calibrated in lineal energy expressed in keV/µm physical units.

NOTE1. After the 0X scaling, it is necessary re-normalize the dose spectrum to obtain ***d(y)*** and hence the correct ***yd(y***) spectrum.

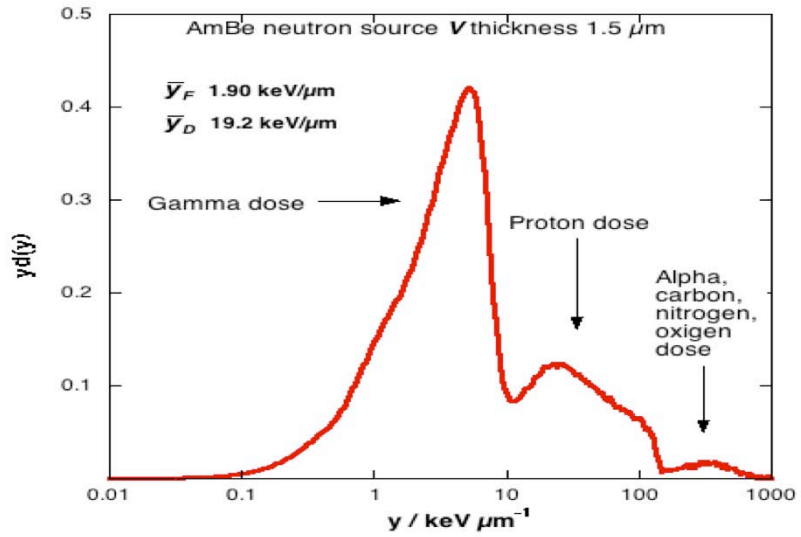
NOTE2. The product ***œ·d(œ)*** as well as the product ***yd(y)*** are dimensionless, since ***d(œ***) and ***d(y)*** are (normalized) count densities with dimension ***1/œ*** and ***1/y*** respectively.

The extrapolation procedure of the microdosimetric spectrum



After the lineal energy calibration, the microdosimetric spectrum has to be corrected (extrapolated) in order to cancel the electronic noise and to include those imparted-energy events that were not measured. The procedure is: **1.** Chose on ***yd(y)*** spectrum a small region just outside the noise peak (0.3 – 0.4 keV/µm in the figure). This data interval is supposed to be due only to the radiation field. **2.** Extrapolate linearly in the ***f(y)*** distribution the experimental points of the selected region to y = 0.01keV/µm (it is about one ionization event in the counting gas of the mini-TEPC) . **3.** Substitute in the ***f(y)*** distribution the the data of y < 0.3 keV/µm with the straight line data. **4.** Re-normalize the new ***f(y)*** spectrum. **5.** Calculate the ***y·f(y)*** spectrum and normalize the product spectrum to obtain ***d(y)***. **6.** Eventually**,** calculate the product spectrum ***y·d(y)***.

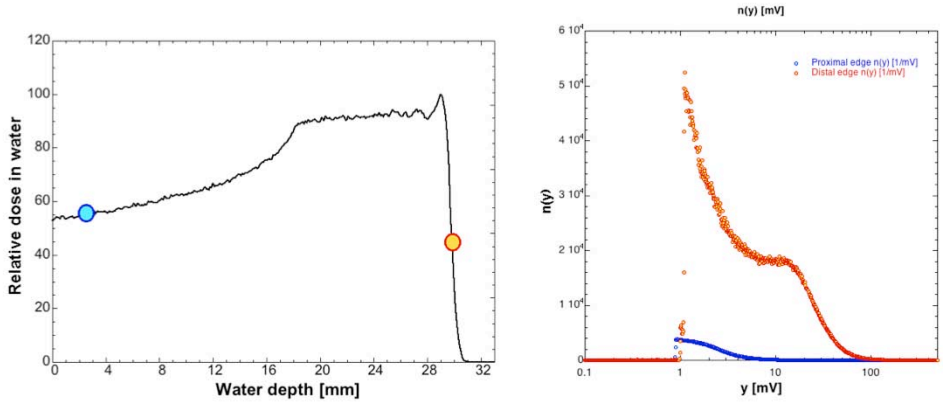
The complete microdosimetric spectrum



The complete microdosimetric spectrum shows three large “hills”, the visual area of which is their relative dose contribution. Calculating the visual areas, we obtain that the absorbed dose is due to gamma rays for the 70%, to protons for the 25% and to light ions for the 5%

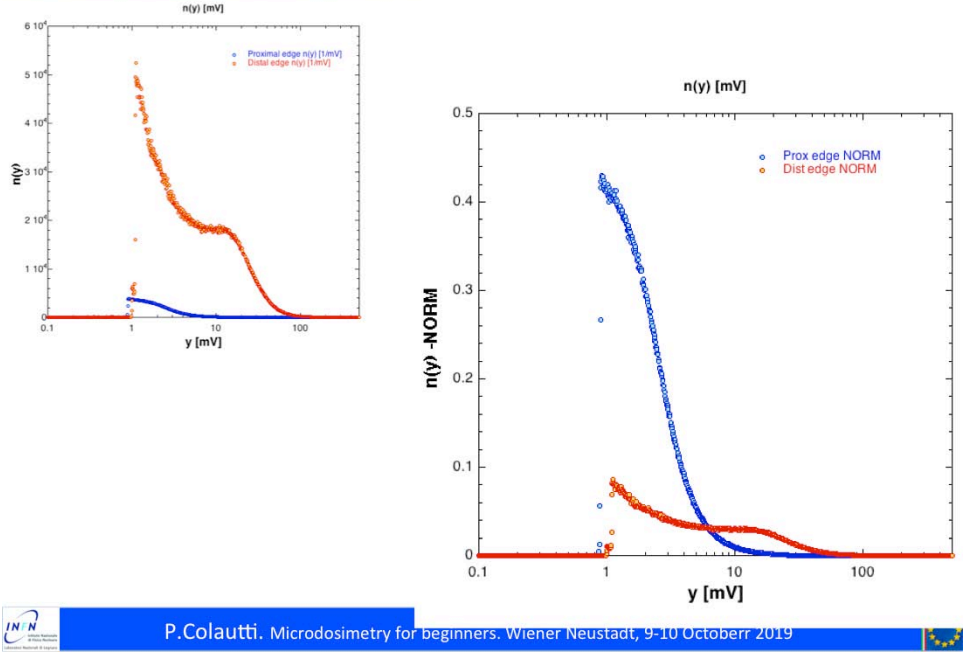
NOTE. Only the mean values of ***f(y)*** and ***d(y)*** of the complete spectrum (that means from 0.01 to ymax) have to be used. The mean values of an incomplete spectrum do not represent the microdosimetric mean values of the equivalent tissue site.

EXERCISE 1st step: open the two files



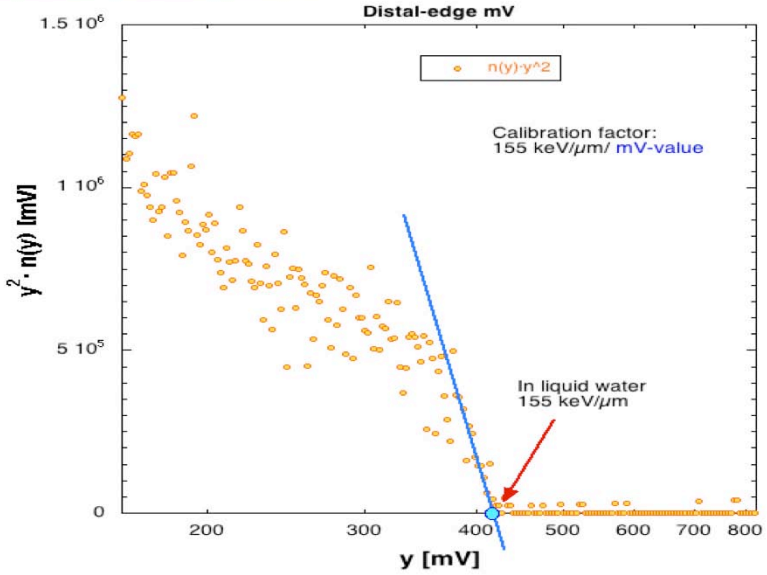
The 2 spectra of data taken at the therapeutic facility of CATANA in the Proximal-Edge (blue circles) and in the Distal-Edge (red circles) of the SOBP used for treating ocular melanoma. The spectra (right side figure) are the results of the junction of 3 sub-spectra after the calibration in mV. The spectra are semi-log. The OX-axis is logarithmic. The original linear data have been compacted in 300 equal intervals per decade. The exercise consists of reading the enclosed spectra (given od two TXT files (first column is the mV channel value, the second column is the number of counts for channel (count number/ mV interval-value of the channel). The exercise continue performing manually all the operation to obtain the two final microdosimetric spectra. In the following, the steps to perform to arrive at the end of the exercise are shown.

EXERCISE 2nd step (OPTIONAL): normalization



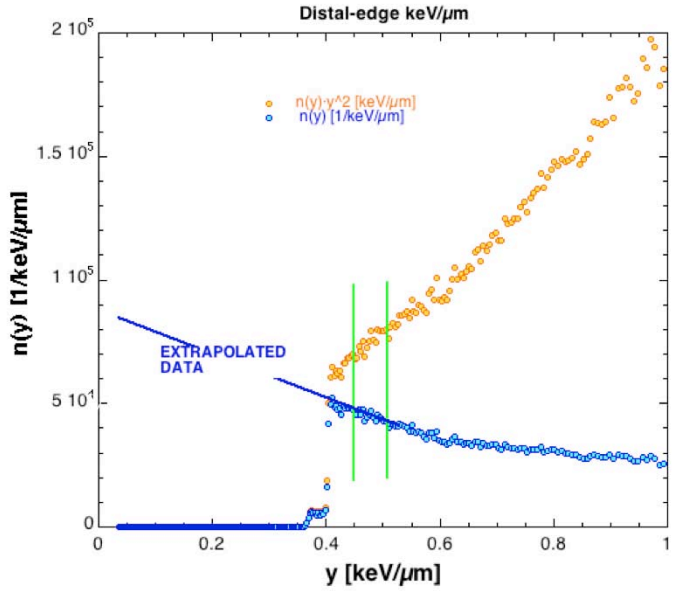
This step is optional. It is useful only to see that the spectra normalised to 1 (the data have to be divided by the spectrum integral value) are correct, since the absolute values of the spectra depend on the counting time.

EXERCISE 3rd step: lineal energy calibration



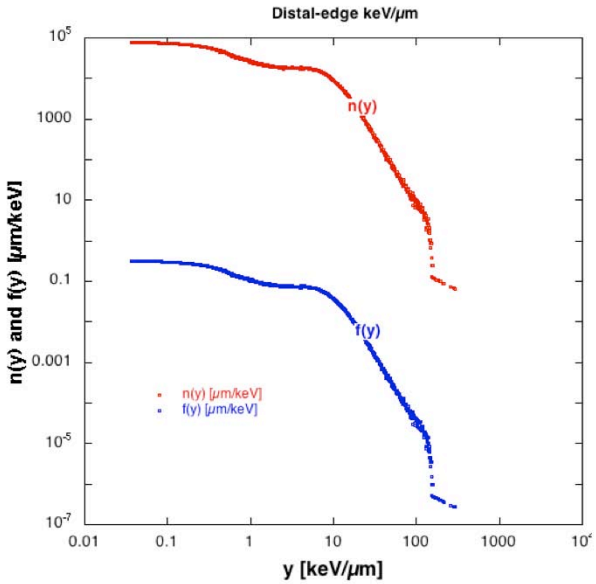
This data-processing step is for for changing the y values from mV values to keV/µm values in liquid water.

EXERCISE 4th step: extrapolation1



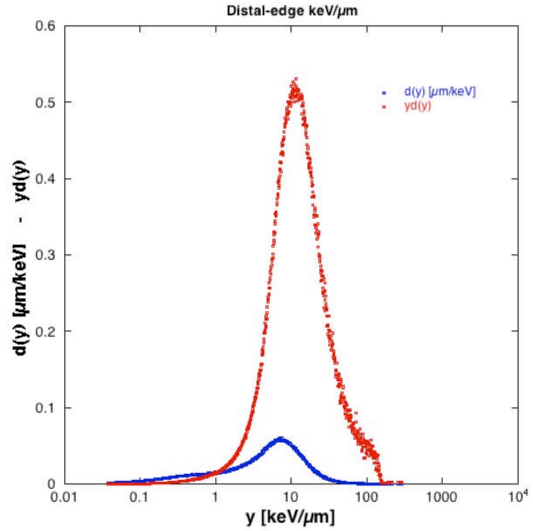
This step is to extrapolating the n(y) data down beyond the detection threshold, down to 0.0keV/µm (~ 1 ionisation event in propane gas).

EXERCISE 5th step: extrapolation2 and normalisation



This step is to normalise the the extrapolated n(y) spectrum. Only after the normalisation the spectrum is called f(y).

EXERCISE 6th step: d(y) and yd(y)



This step is to obtain the d(y) distribution by multiplying f(y) per y and re-normalising again the resulting distribution. Eventually, multiply d(y) per y (without re-normalise again) to obtain the "visual" dose distribution of y. The mean spectral value Y_F and Y_D are calculated by using the f(y) and d(y) distributions respectively.

EXERCISE 7th step: repeat for the proximal edge

After the completion of the “distal-edge” spectrum processing, repeat everything with the “proximal-edge” spectrum. At the 3rd step (calibration), use the calibration factor found for the distal-edge spectrum.