On the Monte Carlo calculation of unrestricted dose-average linear energy transfer distributions in proton therapy

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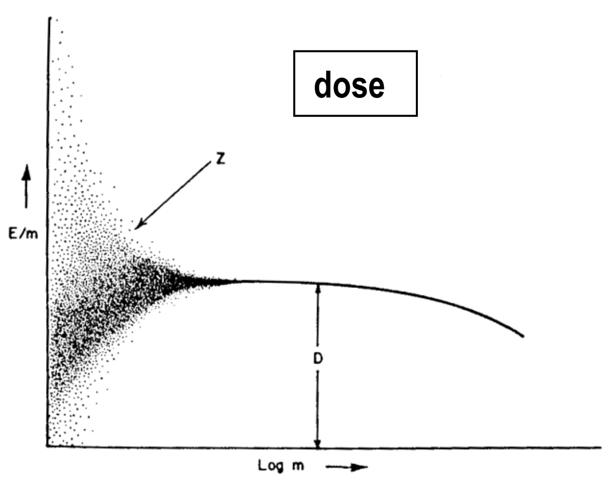
Introduction

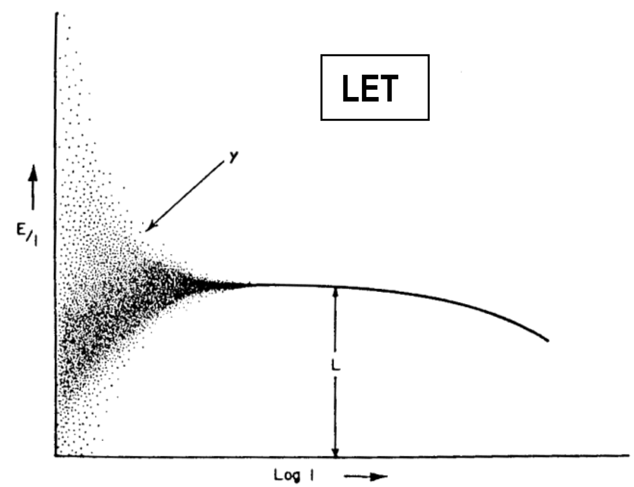
- A key issue in hadrontherapy is the calculation of the **relative biological effectiveness (RBE).**
- RBE varies not only with tissue, cell type or endpoint, but also with the kind of radiation.
- **Track structure** and **linear energy transfer (LET)** are usually used to characterize the incident radiation. In microdosimetry, **lineal energy (*y*)** is the most frequently used quantity for this. The value of ***y*** should tend to **LET** as the sampling volume increases.
- Thus, both **dose** and **LET** distributions have to be taken into account for biological optimization of the treatment planning. Average LET are often used, either **track- (LET_t)** or **dose-averaged (LET_d).**

Aims

1. To compare various **LET$_d$** scoring methods varying voxelization conditions.

2. To show the robustness of each **LET$_d$** scoring method based on **(a)** stability against s changes of simulation parameters (voxel size, production cuts of secondaries) and **(b)** convergence to **dose-mean lineal energy values (y_D)** calculated with equivalent irradiation conditions.





Dose-Average LET

According to **ICRU 16**, **LET$_d$** can be defined as:

$$\overline{L}_{\rm d} = \int L\, d(L)\, {\rm d}L$$

$$\overline{L}_{\rm d} = \frac{\sum_n \left(\frac{{\rm d}E}{{\rm d}l}\right) {\rm d}E}{\sum_n {\rm d}E}$$

Event-by-event basis (Monte Carlo calculations)

Grassberger & Paganetti PMB 56 (2011)

Equivalent

$$\overline{L}_{\rm d}(\mathbf{x}) = \frac{\int_0^\infty \phi_E(\mathbf{x})\, S^2(E)\, {\rm d}E}{\int_0^\infty \phi_E(\mathbf{x})\, S(E)\, {\rm d}E}$$

Average of all particles at a certain point (Analytical calculations)

Wilkens & Oelfke MP 30 (2003)
&
See talk by D. Sánchez-Parcerisa

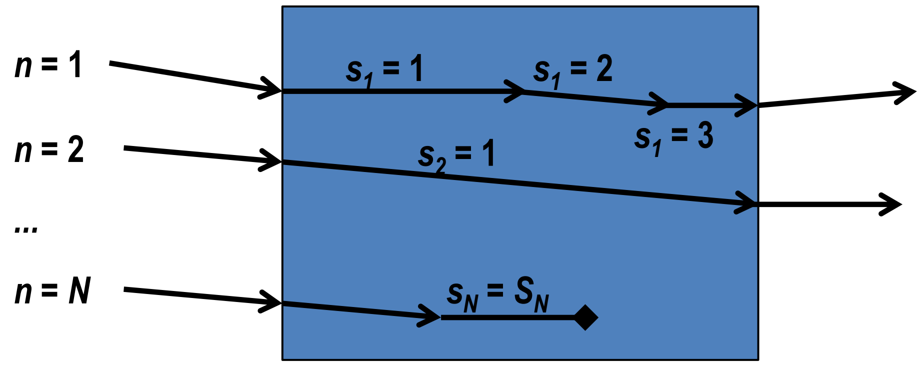
Monte Carlo Calculation of $\mathrm{LET_d}$

$$\bar{L}_{\mathrm{d}} = \frac{\sum_n \left(\frac{\mathrm{d}E}{\mathrm{d}l}\right)\mathrm{d}E}{\sum_n \mathrm{d}E}$$

Event-by-event basis

Consider a certain voxel irradiated by ***N*** tracks:

- Each track ***n*** makes ***S_n*** steps within the voxel.
- We focus on primary protons only.



- ***n*** = track index
- ***s*** = step index

LET$_d$ Scoring Methods Proposed

$$\bar{L}_d = \frac{\sum_n \left(\frac{dE}{dl}\right) dE}{\sum_n dE}$$

Method #1 (A)

$$\bar{L}_d = \frac{\sum_{n=1}^{N} \sum_{s=1}^{S_n} \omega_n \frac{\varepsilon_{sn}^2}{l_{sn}}}{\sum_{n=1}^{N} \sum_{s=1}^{S_n} \omega_n \varepsilon_{sn}}$$

Step-by-step computation of the actual **d*E*/d*l*** of each proton

Method #2 (B)

$$\bar{L}_d = \frac{\sum_{n=1}^{N} \left[\omega_n \frac{\left(\sum_{s=1}^{S_n} \varepsilon_{sn}\right)^2}{\sum_{s=1}^{S_n} l_{sn}} \right]}{\sum_{n=1}^{N} \left[\omega_n \sum_{s=1}^{S_n} \varepsilon_{sn} \right]}$$

Computation along the voxel of the actual **d*E*/d*l*** of each proton

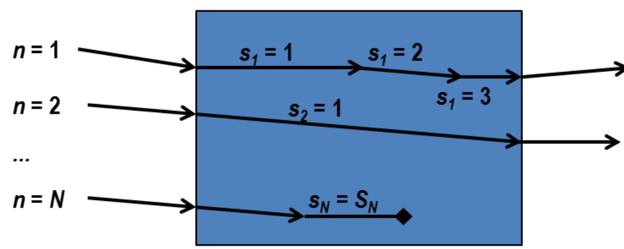
Method #3 (C)

$$\bar{L}_d = \frac{\sum_{n=1}^{N} \sum_{s=1}^{S_n} \omega_n L_{sn} \varepsilon_{sn}}{\sum_{n=1}^{N} \sum_{s=1}^{S_n} \omega_n \varepsilon_{sn}}$$

L_{sn} is the average **d*E*/d*l*** (i.e., as one would obtain from tables) according to particle type, energy and target material (step-by-step computation)

- **ω = track weight**
- **ε = electronic energy loss per step(*)**
- **l = step length**

(*) Kinetic energy of all secondary electrons included in ε (unrestricted LET)



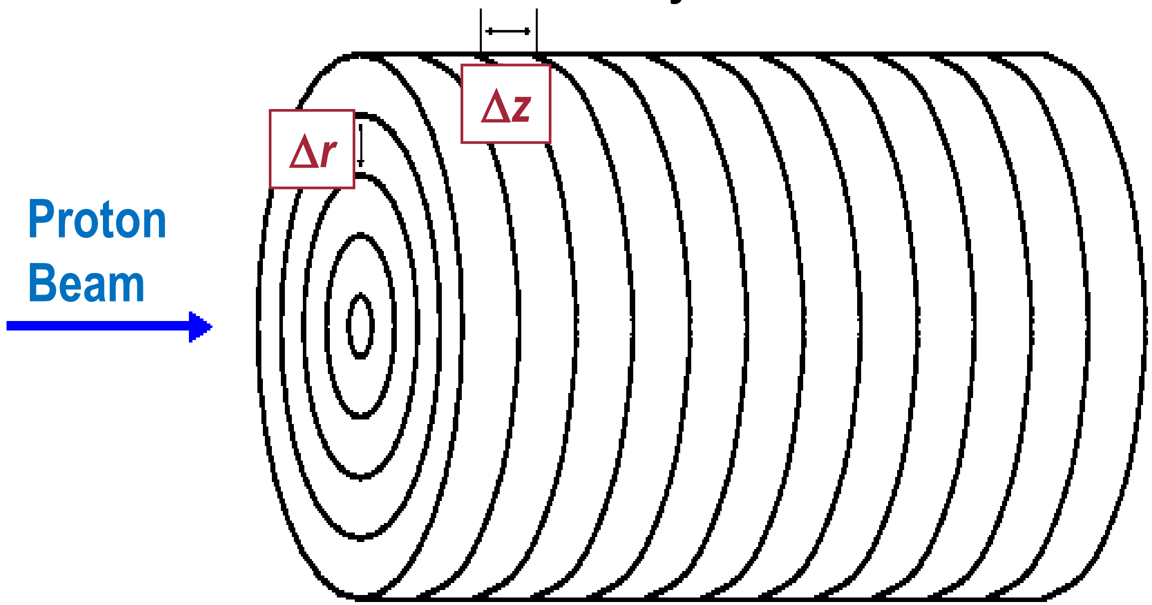
Cortés-Giraldo & Carabe, PMB 60: 2645 (2015)

LET_d Calculation Setup

Dose and LET_d simulation with Geant4 (v9.6.2)

Geometry

Proton Beam



- Water tank – cylindrical symmetry
- Δz = 0.2 – 2.0 mm
- Δr = 2.0 – 5.0 mm
- LET_d of primary protons only (to ease comparison between techniques).

Physics List

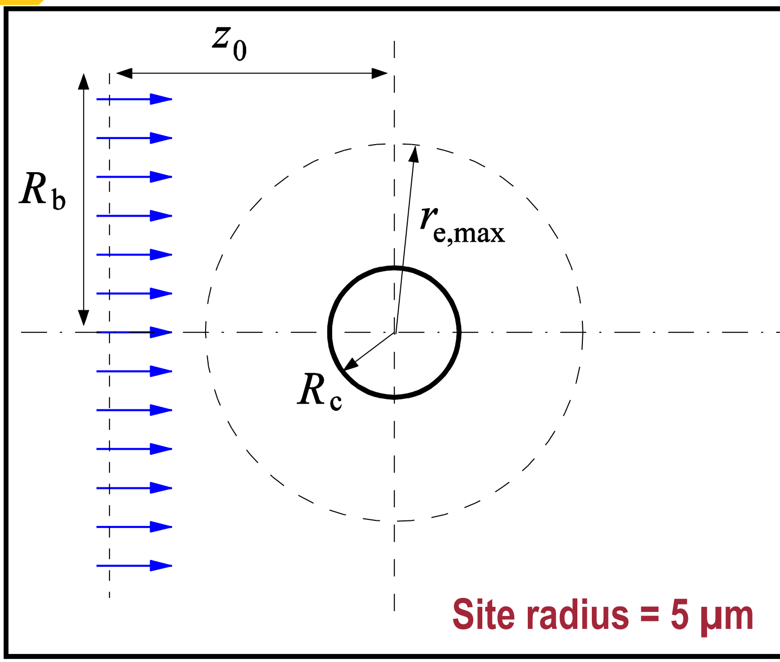
- StandardEM_option3
- QGSP_BIC_HP
- Prod. cut = 0.05 mm

Proton Beams

- 160 MeV beamlet
- Clinical SOBPs

Microdosimetry Calculations

Lineal energy calculations



- Circular uniform proton beam, larger than maximum range of secondary e-.
- Proton **energy spectrum taken from the macroscopic calculation** (previous slide) at the depth of interest.
- **Penelope EM physics list** for e- and gammas (cut = 0.7 μm, 100 eV approx. in water).

Lineal energy

$$y = \frac{\varepsilon_s}{\bar{l}}$$

Energy imparted

$$\varepsilon = \sum_i \varepsilon_i$$

Mean chord length

$$\bar{l} = \frac{4V}{A}$$

Frequency-mean lineal energy

$$\bar{y}_F = \int_0^\infty y\, f(y)\, \mathrm{d}y$$

Dose-mean lineal energy

$$\bar{y}_D = \int_0^\infty y\, d(y)\, \mathrm{d}y = \frac{1}{\bar{y}_F} \int_0^\infty y^2 f(y)\, \mathrm{d}y$$

Link Between Micro- and Macroscopic Calculations

A.M. Kellerer, "Fundamentals of microdosimetry" (1985)

$$\bar{y}_{\mathrm{D}} = \frac{9}{8}\bar{L}_{\mathrm{d}} + \frac{3\delta_2}{2d}$$

Assumptions:

- Straight lines are assumed for protons trajectories.
- Residual range significantly larger than site diameter.

Where:

- ***d*** is the site diameter.
- δ_2 represents the weighted average of the energy loss per collision, ε_c, of the traversing charged particle:

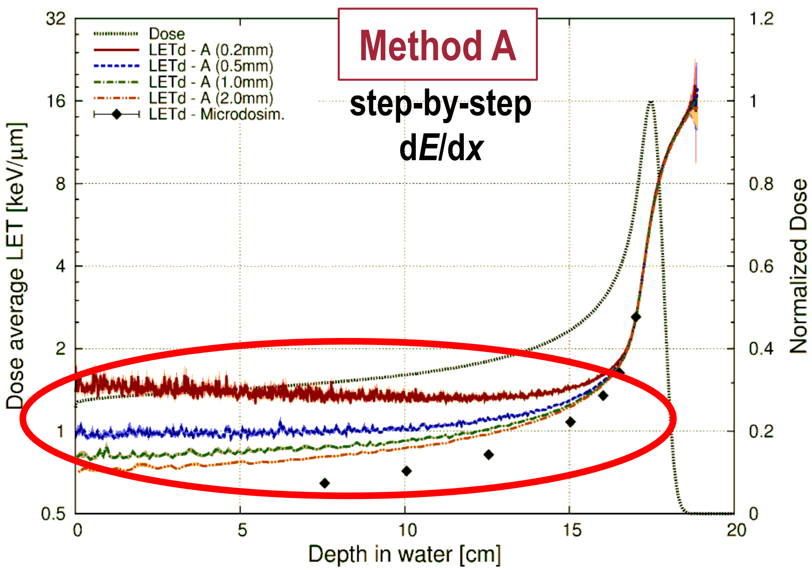
$$\delta_2 = \frac{\int \varepsilon_{\mathrm{c}}^{2}\, f_{\mathrm{c}}(\varepsilon_{\mathrm{c}})\,\mathrm{d}\varepsilon_{\mathrm{c}}}{\int \varepsilon_{\mathrm{c}}\, f_{\mathrm{c}}(\varepsilon_{\mathrm{c}})\,\mathrm{d}\varepsilon_{\mathrm{c}}} \approx \frac{E_d}{2\ln(E_d / I)}$$

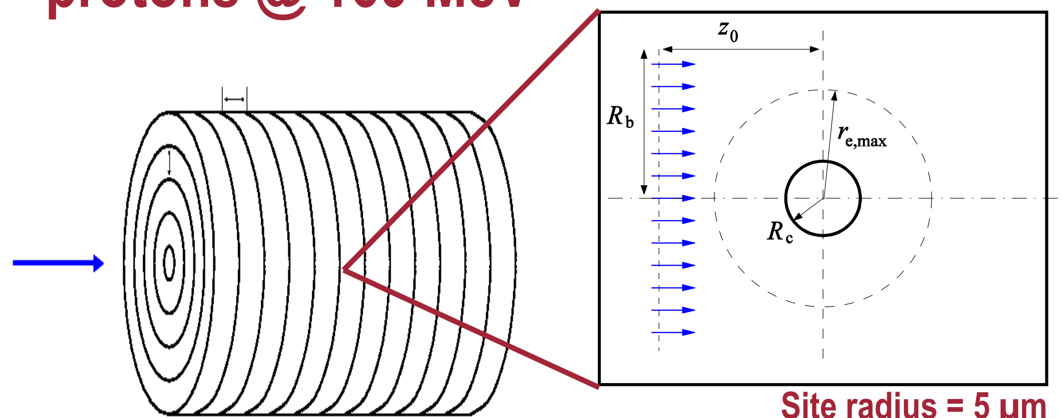
- E_d is an estimated energy – it roughly equals the kinetic energy of e- having range similar to the site diameter.

Results

LET$_d$ Calculations – Stability Against Voxel Size

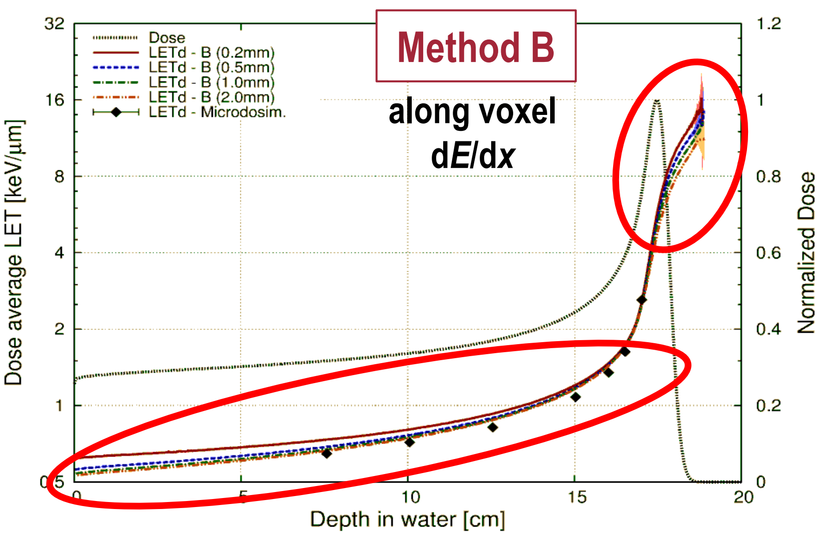
protons @ 160 MeV

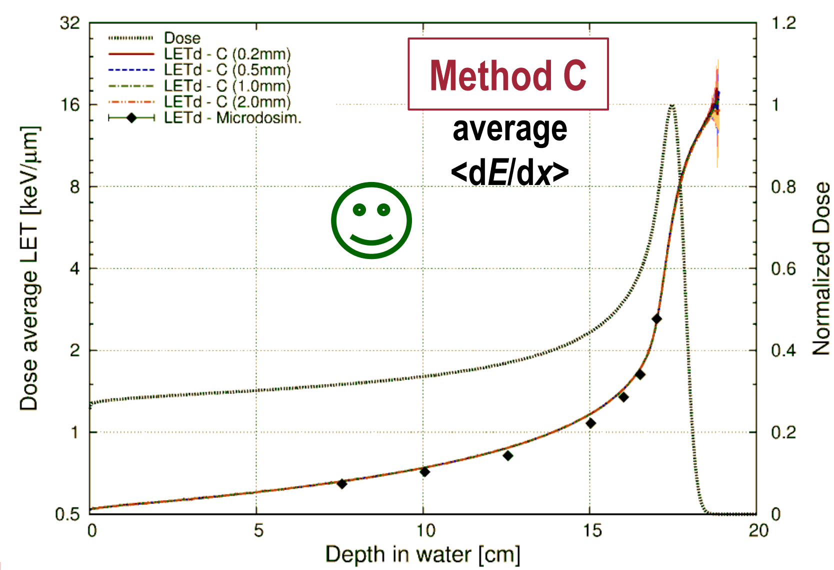




Central axis LET – integrated over 5 mm

Site radius = 5 µm



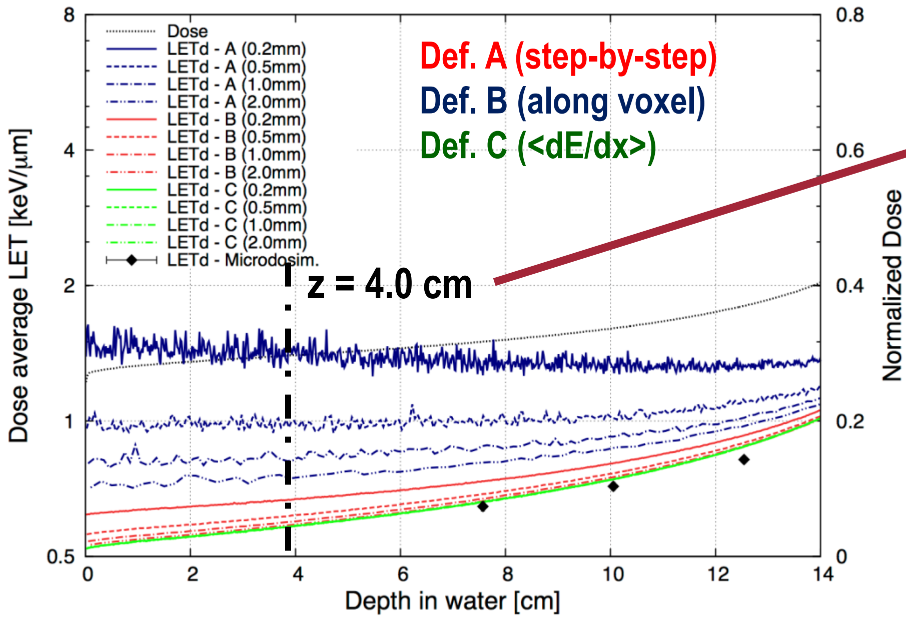


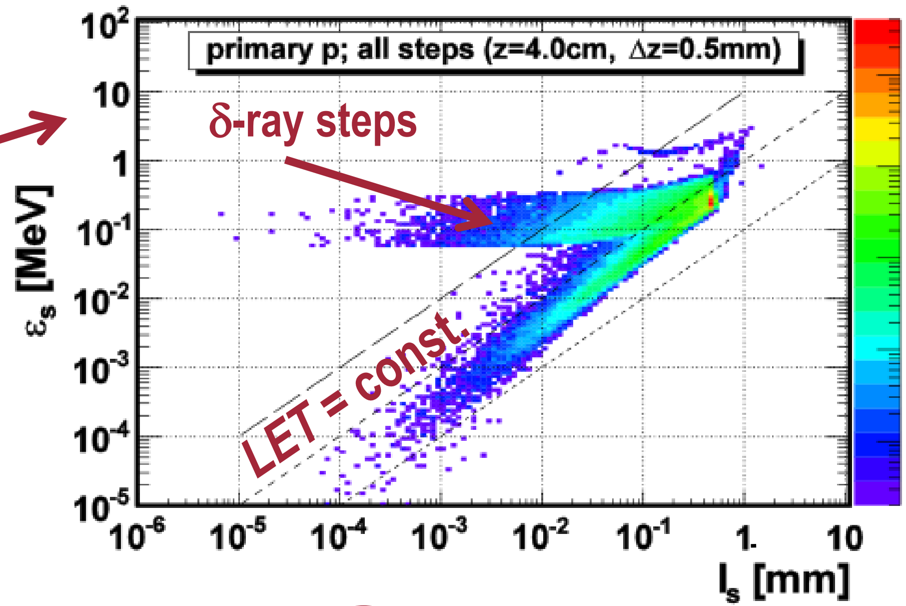
Please note y-axis logscales!

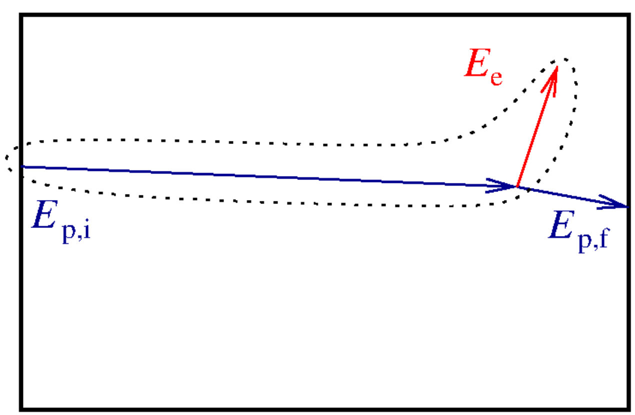
Results

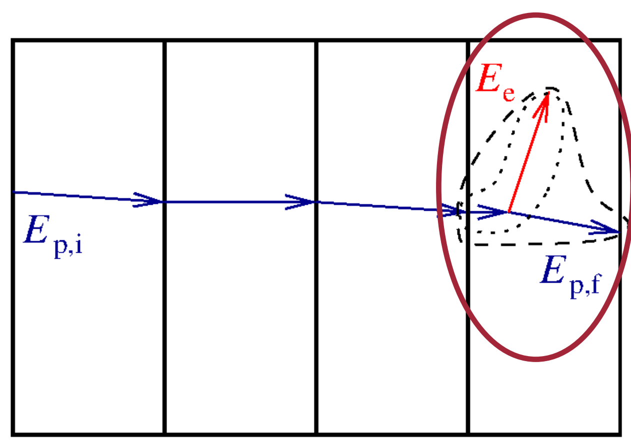
LET$_d$ Calculations – Sensitivity with Voxel Size

Differences at entrance region









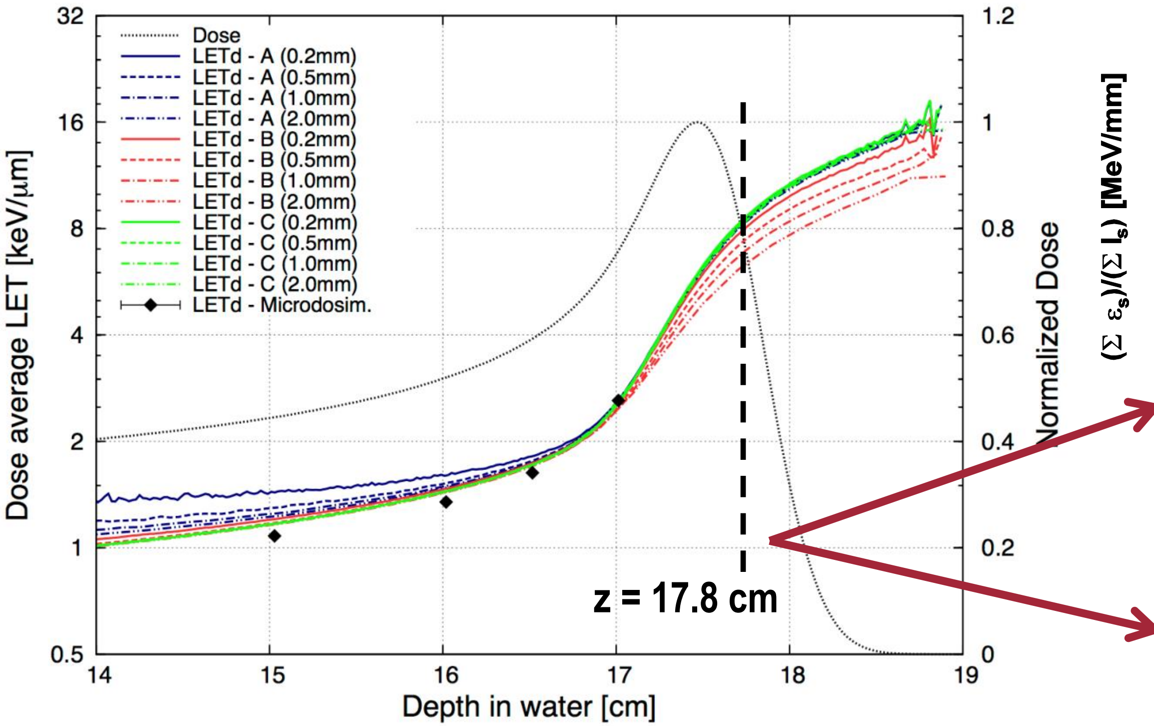
Same physical situation, boundary crossing causes a 'spurious' high LET value when using methods A (dotted step) and B (dashed region)

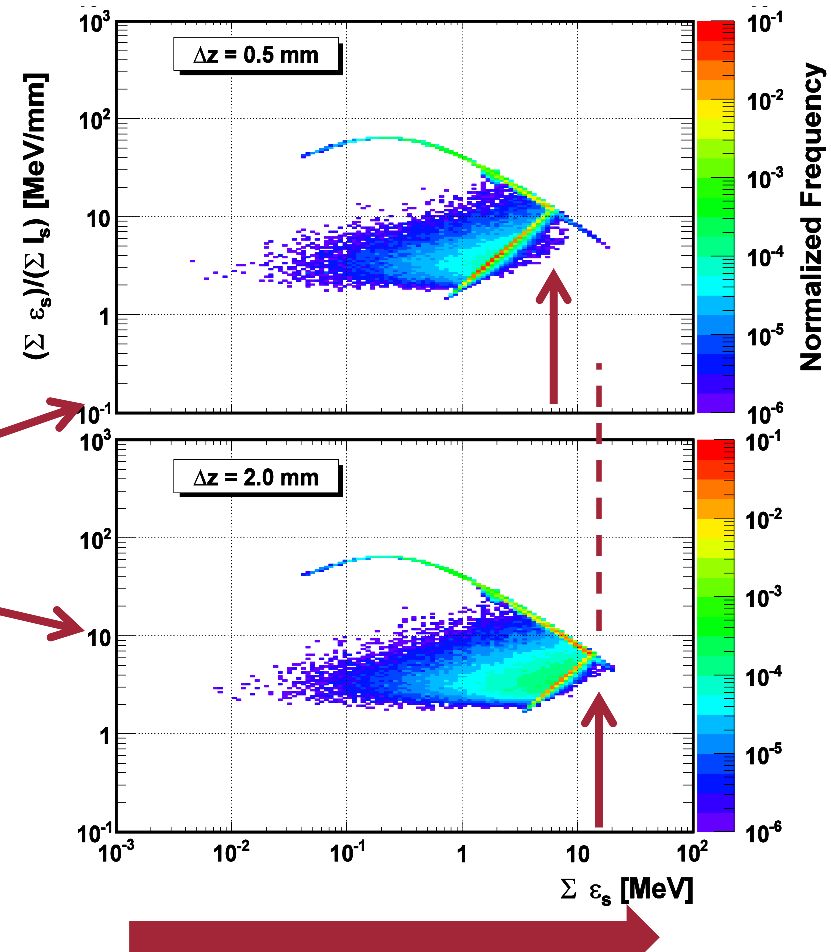
Cortés-Giraldo & Carabe, PMB 60: 2645 (2015)

Results

LET_d Calculations – Sensitivity with Voxel Size

Differences at the Bragg peak region

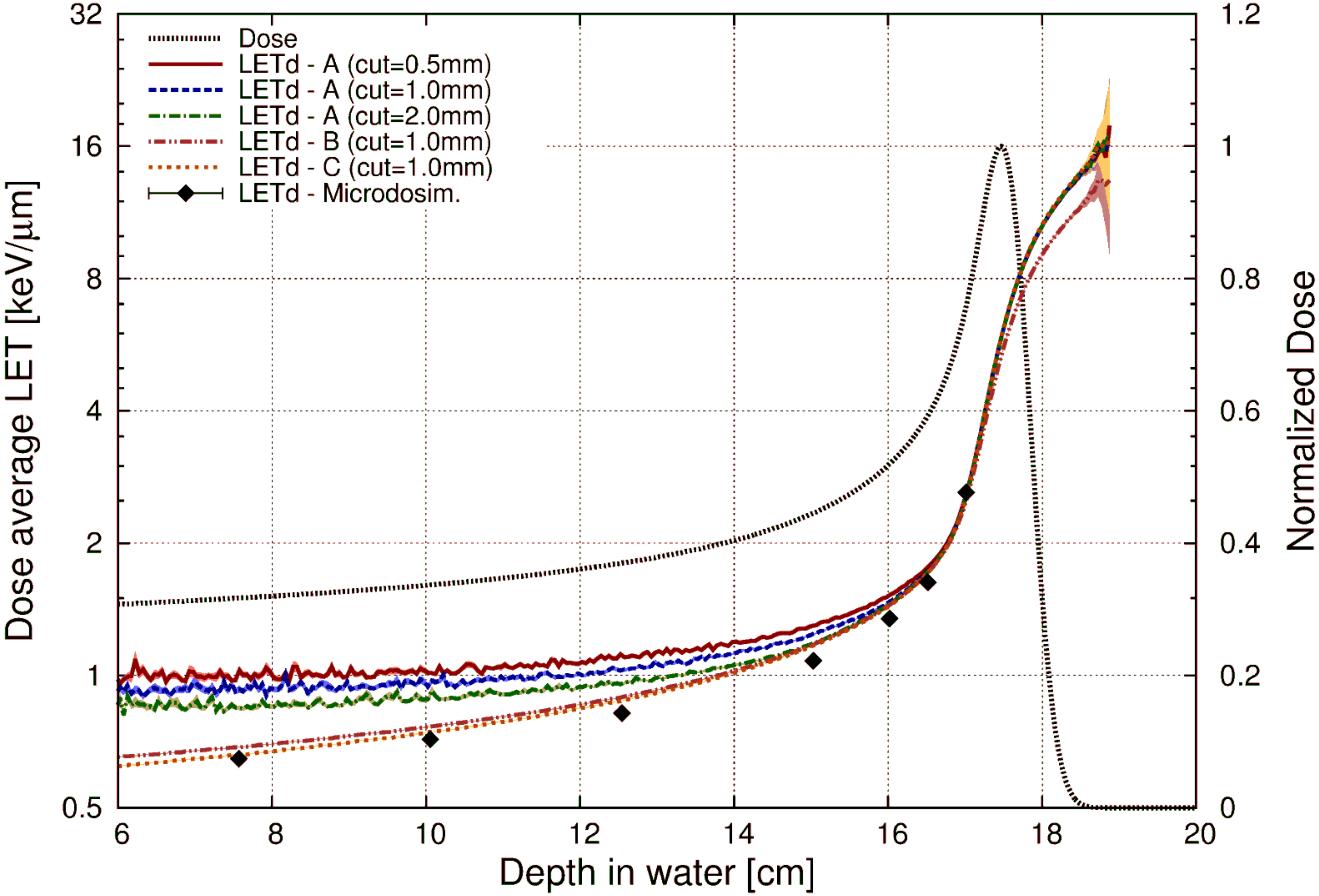




Increasing weighting factor (Method B)

Systematic deviation of the ***LET_d*** value when computing the proton LET along the voxel –
a larger voxel size implies more primary protons stopping within the voxel

LET_d Calculations
Production Cut of Secondary electrons

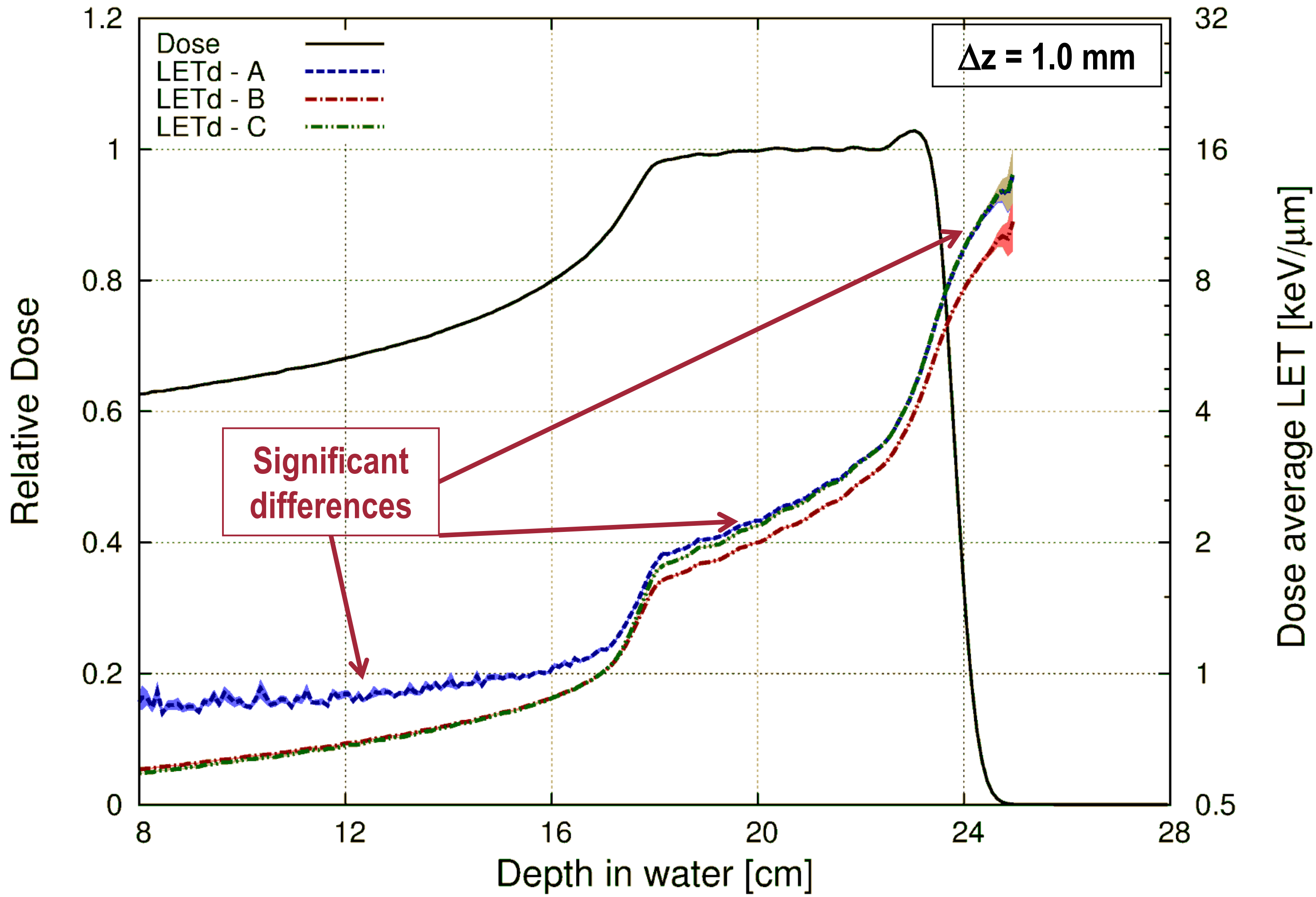


Methods B & C are stable against production cut changes between 0.5 – 2.0 mm.

Method A shows an increasing bias of LET_d as tracking of secondary electrons increases in detail.

Results – LET$_d$ Calculations

Spread-Out Bragg Peak (SOBP)



Cortés-Giraldo & Carabe, PMB 60: 2645 (2015)

Conclusions

- Different Monte Carlo implementation of ***LET_d*** lead to significant deviations in the calculated values, especially at the Bragg Peak region.
- Systematic variations of the calculated ***LET_d*** with varying voxel size along the beam direction due to spurious high LET calculations associated to ‘hard’ collisions.
- These differences resulted in significant deviations when calculating ***LET_d*** distributions for a clinical SOBP.
- **Method C** is recommended for ***LET_d*** calculations, as it is stable against voxel size changes and shows more consistent values with respect to estimated ***LET_d*** from microdosimetry calculations.
- Regardless the method used, calculations need to be contrasted with actual measurements..

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Thanks for your attention!