Clínica Universidad de Navarra

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA E INNOVACIÓN

Ciemat Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas

On the need of using MC Simulations to analyze and minimize the uncertainty of RBE as a function of LET in clonogenic assays

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Background:

Clonogenic assays to determine the **Relative Biological Effectiveness (RBE) for protons** as a function of its **Lineal Energy Transfer (LET).**

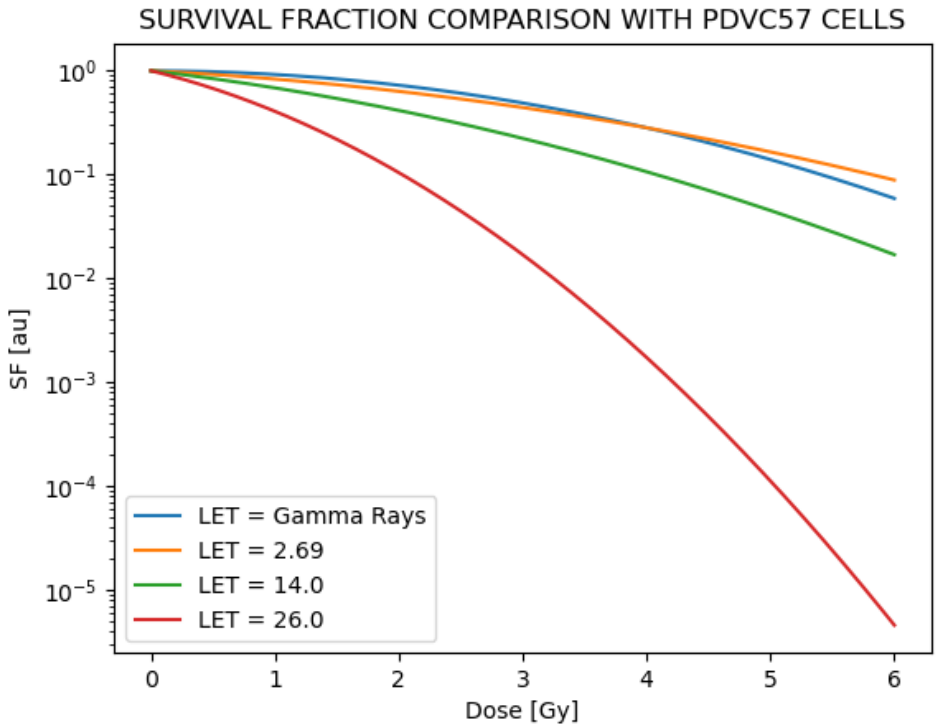
For this aim, we compare **cell survival** irradiated with **high energy X-Rays** and with **protons** at the same dose.

CELL LINES CULTURE:

- Fibroblast hamster lung
- Human Lung Carcinoma
- Human glioblastoma
- Mouse breast carcinoma
- Mouse renal carcinoma

IRRADIATION with **X-RAYS** and **PROTONS** at different **LET values**

$$RBE = \frac{Dp}{D\gamma}$$



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Current Limitations:

- Published results of clonogenic assays show a big variability between them
- In the many reviewed articles, the uncertainty is not specified or explained in detail
- This hinders the modeling of phenomenological RBE models as a function of dose, LET and α/β and therefore its potential application in clinical treatments

Our aims:

1. Take into account all factors contributing to RBE measurement uncertainty
2. Optimize experimental setup to reduce the uncertainty

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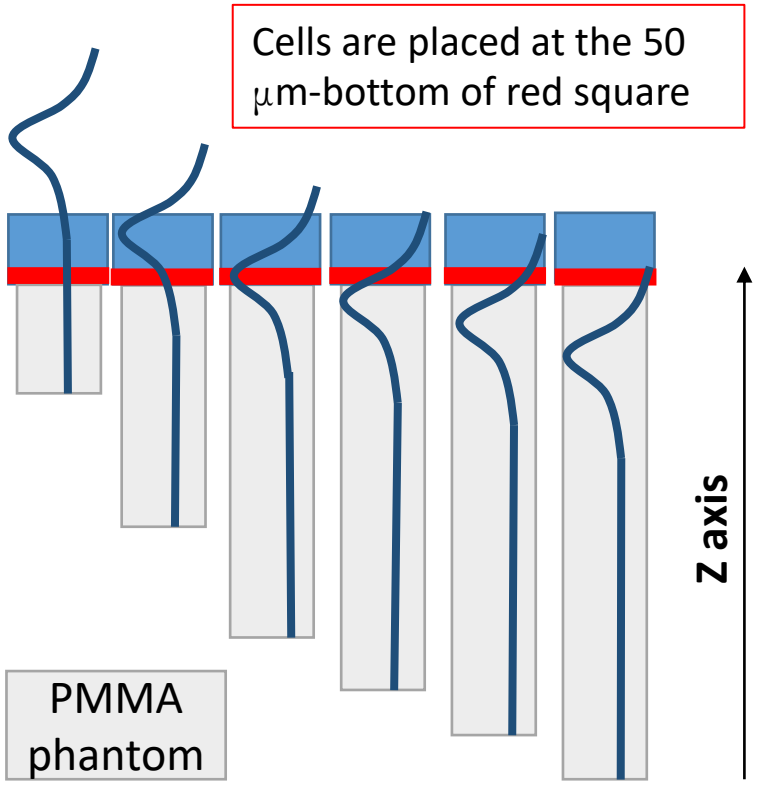
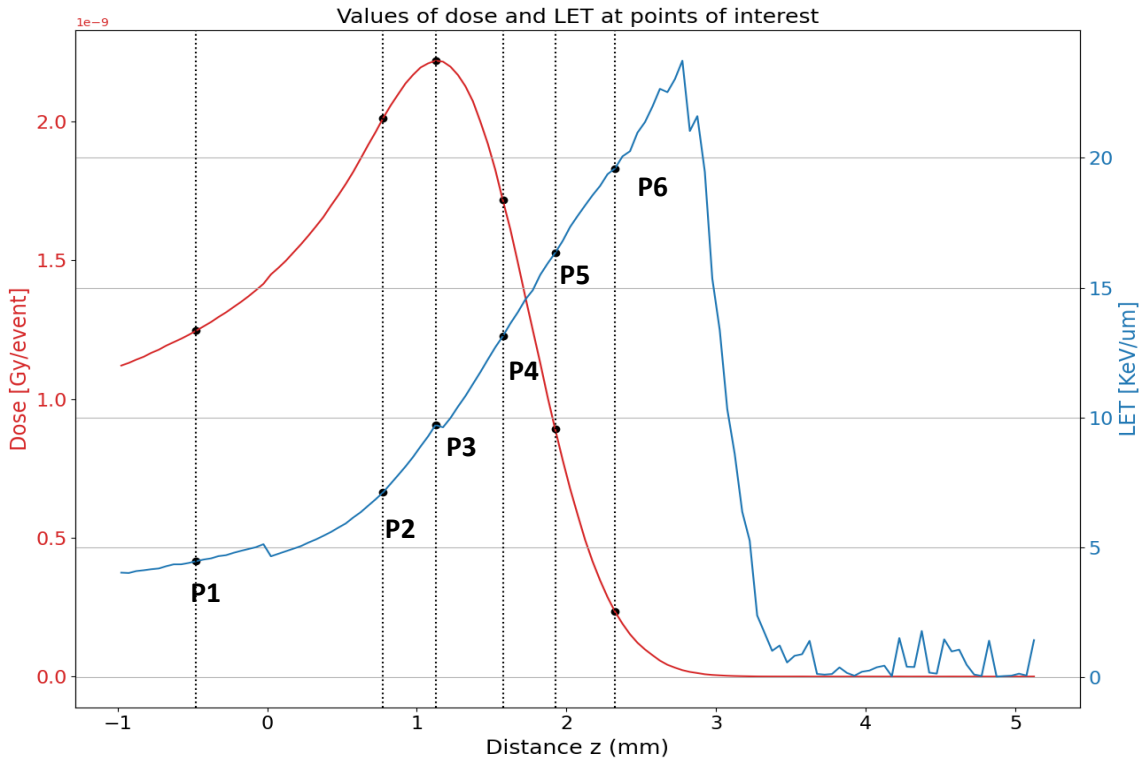
Method:

1. Irradiation at different LET/dose points:



2. Detailed beam Simulation with GAMOS/Geant4 of experimental setup
   - Commercial TPS cannot be used



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What do we need from the proton beam?

- The **optimum beam energy:**
  1. High LET values at the end of the profile
  2. Homogeneous Dose for all cells in a well
  3. Homogeneous LET for all cells in a well
  4. Accurate selection of LET points

- 1st , 2nd and 3rd points are optimized at **minimum energy of 70.2 MeV**.
- The 4th, however, is worse at this energy. Despite of this, minimum energy is commonly chosen.

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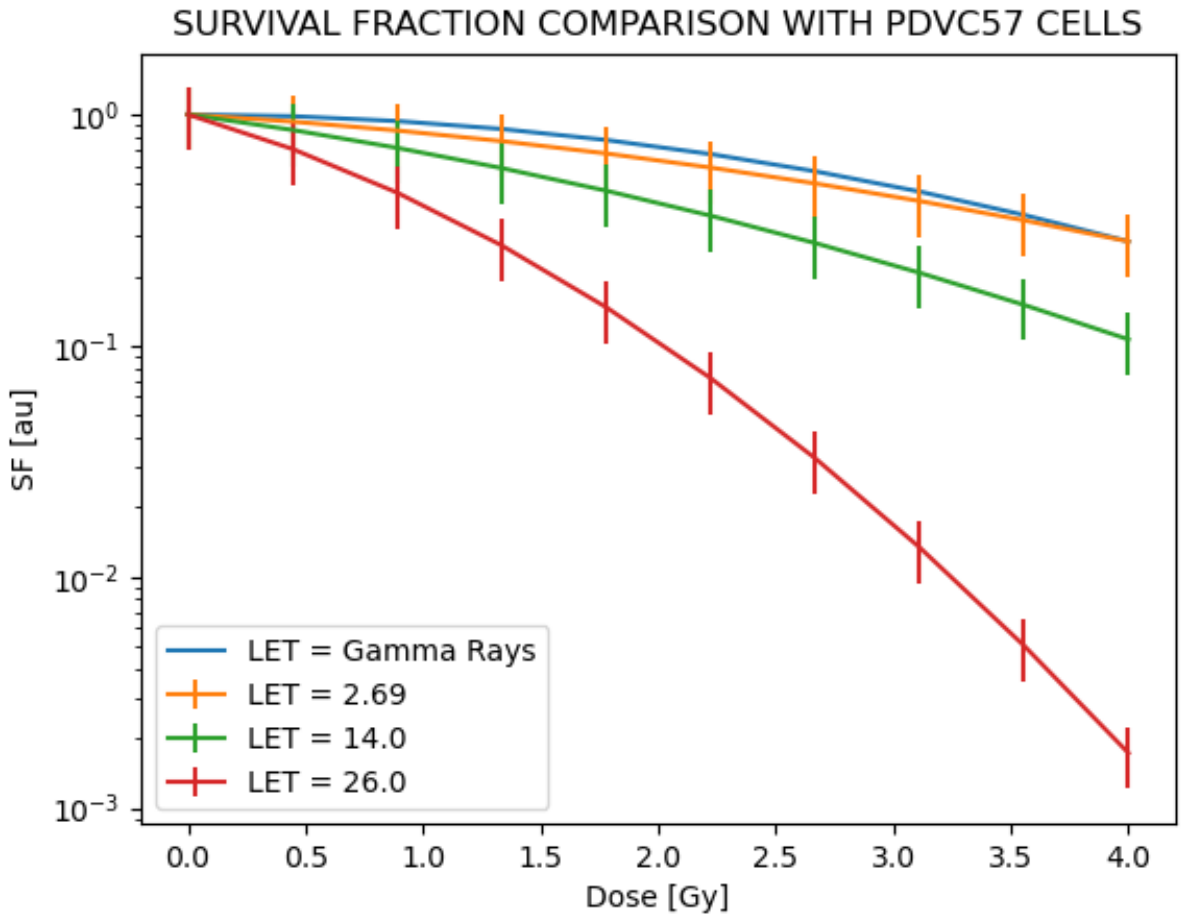
Main Factors contributing to RBE uncertainty:

1. Biology:

Cell Survival uncertainty is up to 20-30% !



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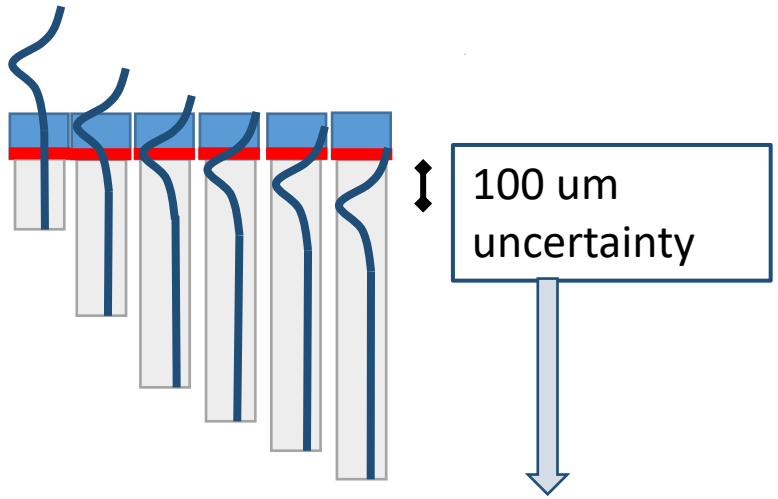
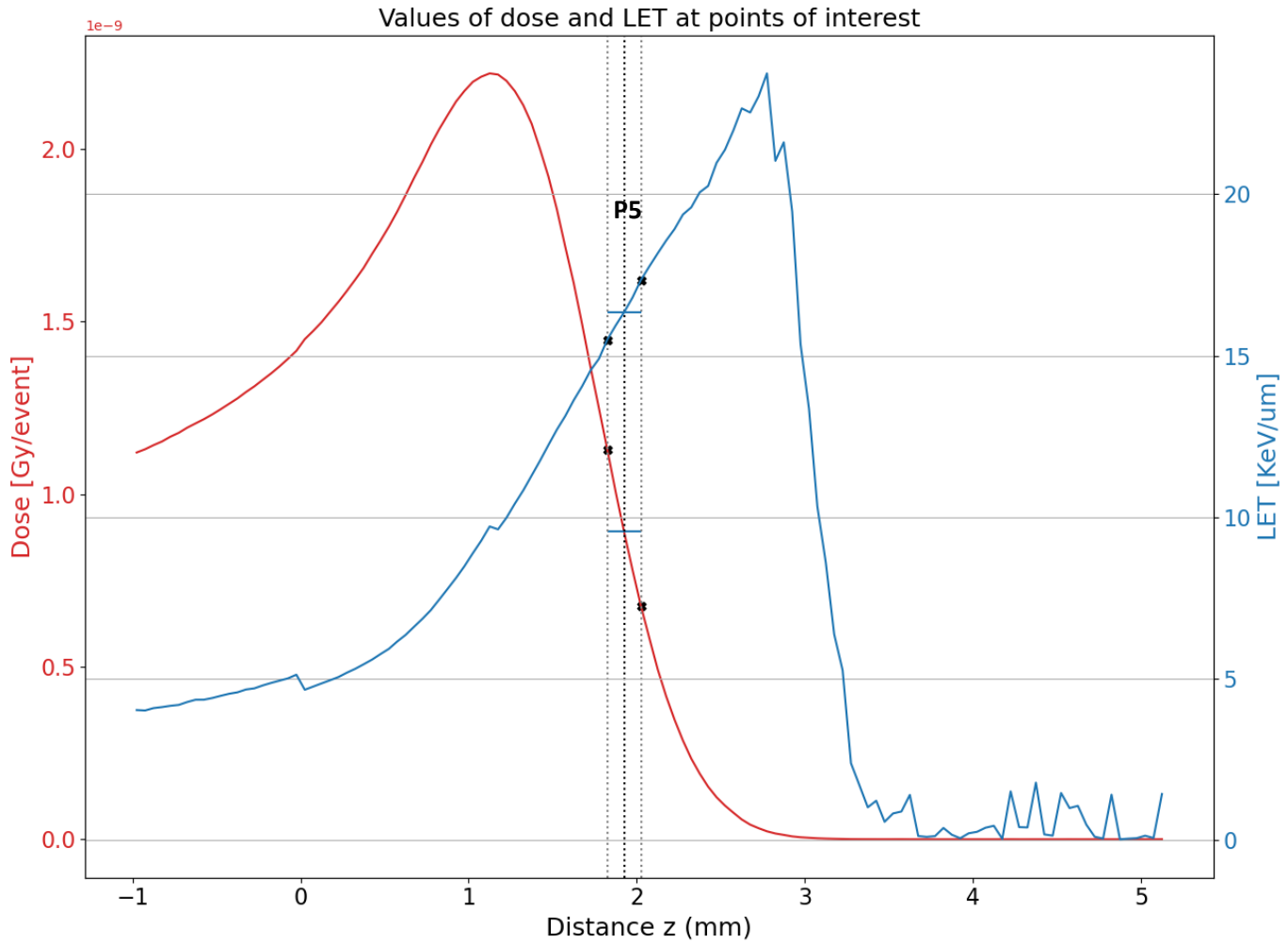
2. From the dose experimental measurements:

Uncertainty in the Bragg curve position



Dose Uncertainty of ~9%
LET value Uncertainty of ~6 %



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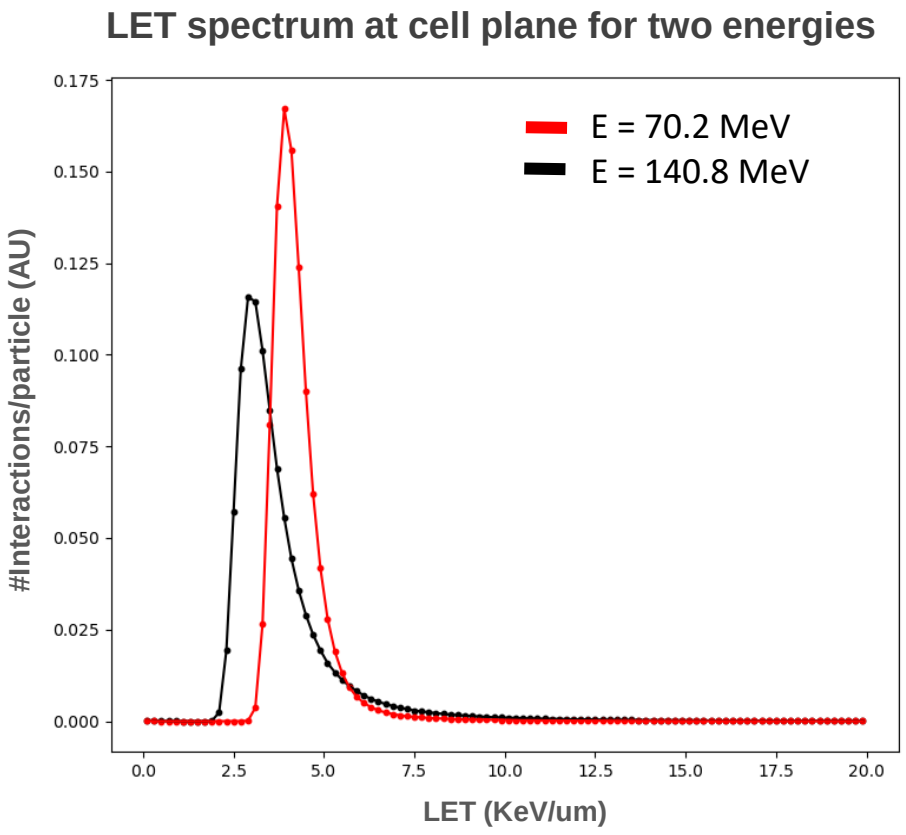
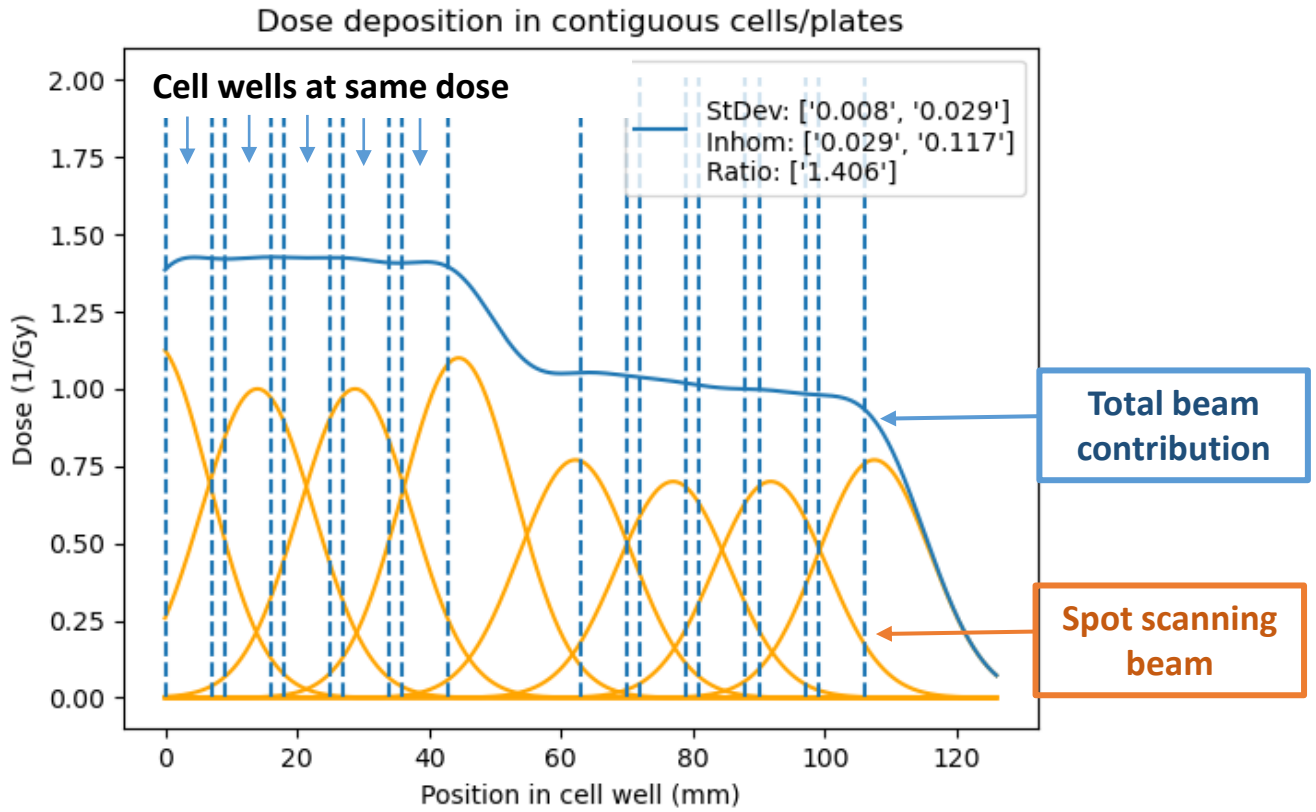
3. From the beam shape at the cell plane:





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Automatic Tool:

Inputs

- Dose, LET, SFx values
- Dose, LET, SFx uncertainties
- α_x and β_x

Phenomenological model
McNamara et al.
Wedenberg et al.
Carabe et al.

SFp values
SFp uncertainty

Output

- α_p and β_p parameters with **uncertainty**
- RBE values with propagated **uncertainty**

- Take the parameters that ensure that the **final uncertainty** is not bigger than a given value:
  - Minimum SF measured
  - Minimum Number of dose points
  - Optimal Dose values

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Conclusions:

- We have used a GAMOS/Geant4 simulation to obtain:
  - RBE values **with uncertainties** to contribute to the development of phenomenological models
  - **Optimal experimental setup** that minimizes the total uncertainty
- A free automatic tool for the scientific community that considers the main contributions to RBE final uncertainty

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