First microdosimetric characterization of nuclear interaction events, and assessment of their effect on the dose-mean lineal energy uncertainty.

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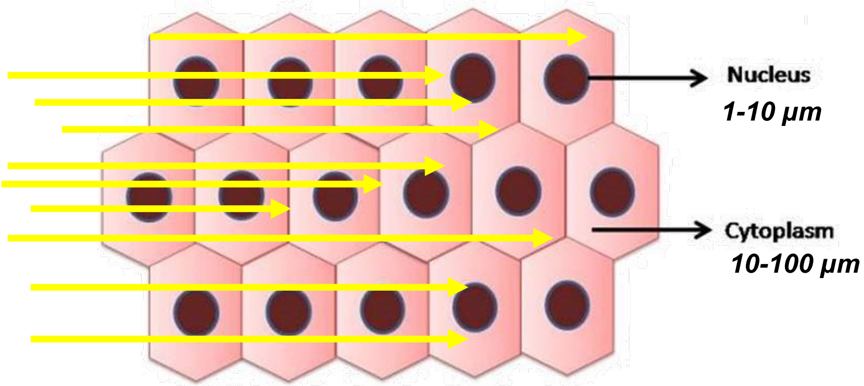
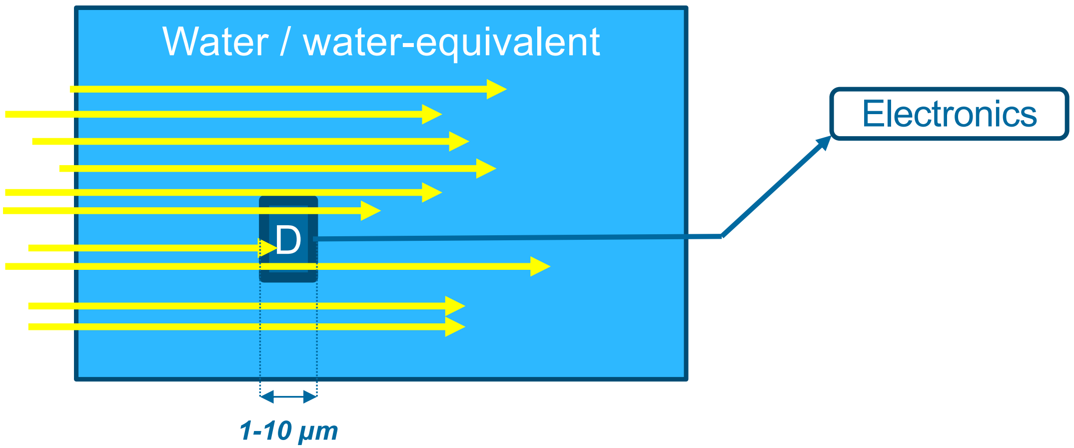
Brief Introduction to Microdosimetry





Investigate the **stochastic** nature of radiation-matter interaction in **cell-like volumes**

↓

Single-event energy deposition

↓

Lineal energy ***y***

$$y = \frac{\varepsilon_S}{\bar{l}} \left[\frac{keV}{\mu m}\right]$$

$\bar{l}$ = mean path length

- Frequency distribution (p.d.f.): $f(y)$
  - $\bar{y}_F = \int_0^\infty y f(y) dy$
- Dose distribution: $d(y) = \frac{y}{\bar{y}_F} f(y)$
  - $\bar{y}_D = \int_0^\infty y d(y) dy = \frac{1}{\bar{y}_F} \int_0^\infty y^2 f(y) dy$

Brief Introduction to Microdosimetry

Measure the energy deposited by the particle in a cell / chromosome like volume

Deeply related to biological effects.

Direct link to radiobiology!

Microdosimetry use in clinical hadron therapy.

To **improve treatment planning** with a more accurate evaluation of RBE and radiobiological outcomes.

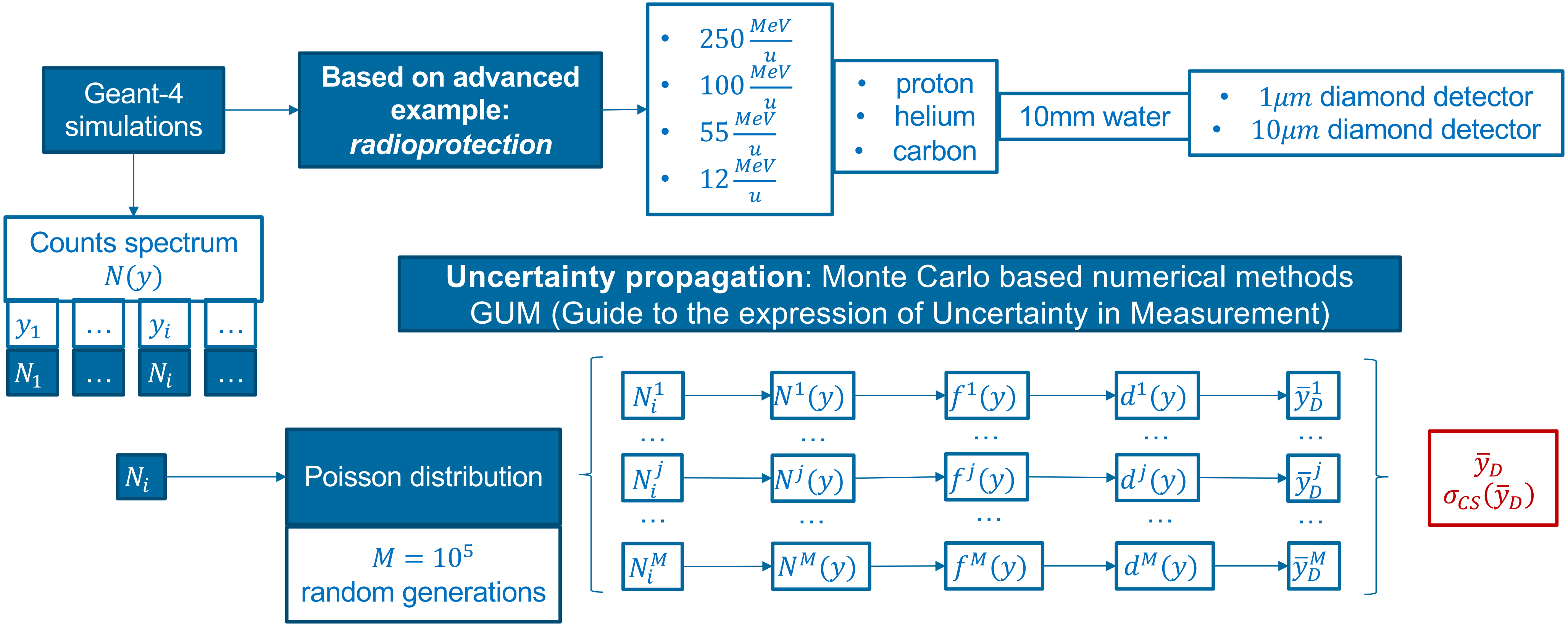
Characterise radiation quality in a unique way

As a **quality assurance** tool

Many different technologies
G. Parisi, F. Romano and G. Schettino, 2022, Frontiers in Physics

Missing standard protocols and code of practice!

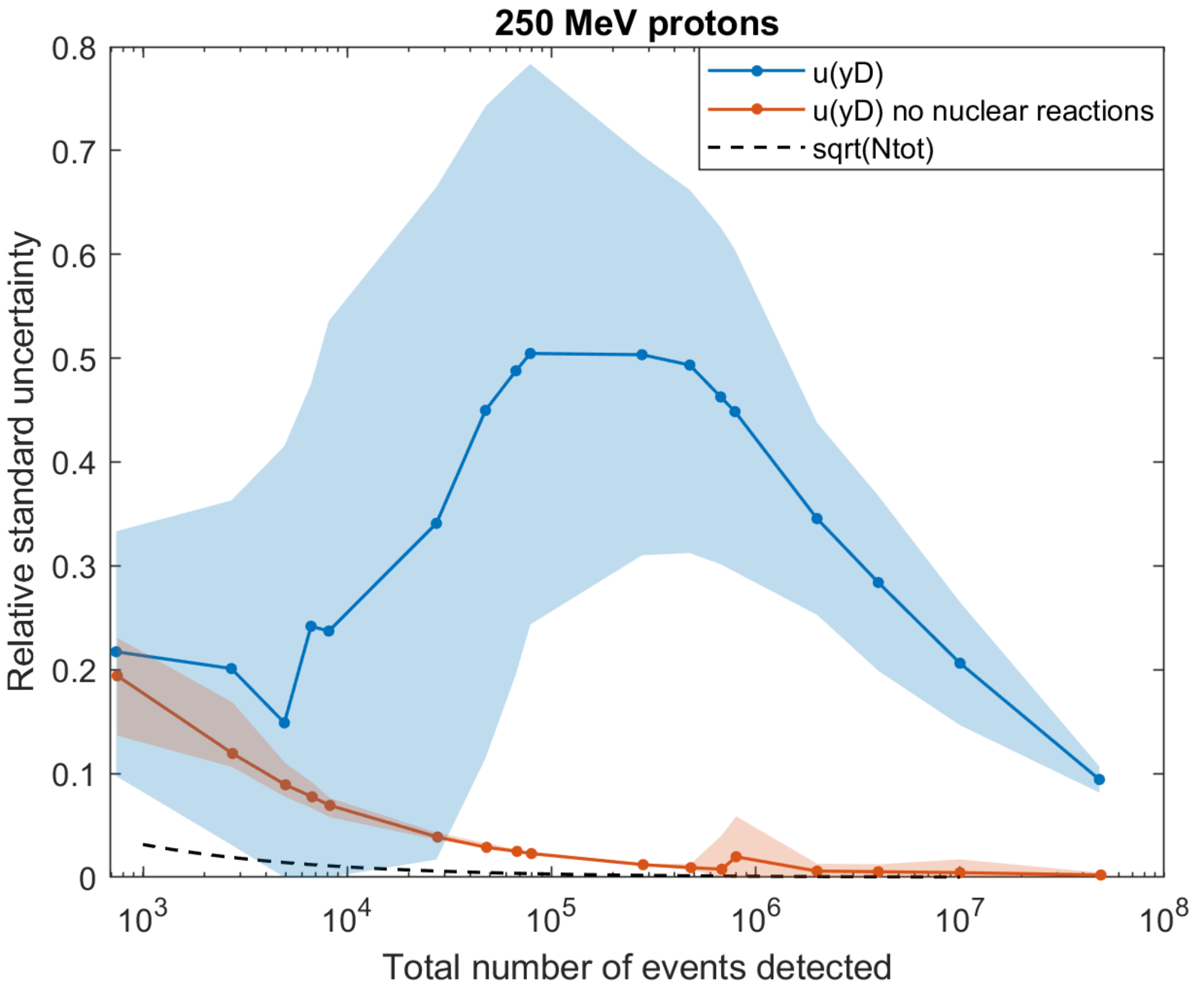
Uncertainty analysis: counting statistics contribution



All this process **repeated** 50 times to account for:

- $\sigma_{CS}(\bar{y}_D)$ variability
- Effect of rare events at low "total number of counts"

Nuclear Interactions influence on $\bar{y}_D$ uncertainty

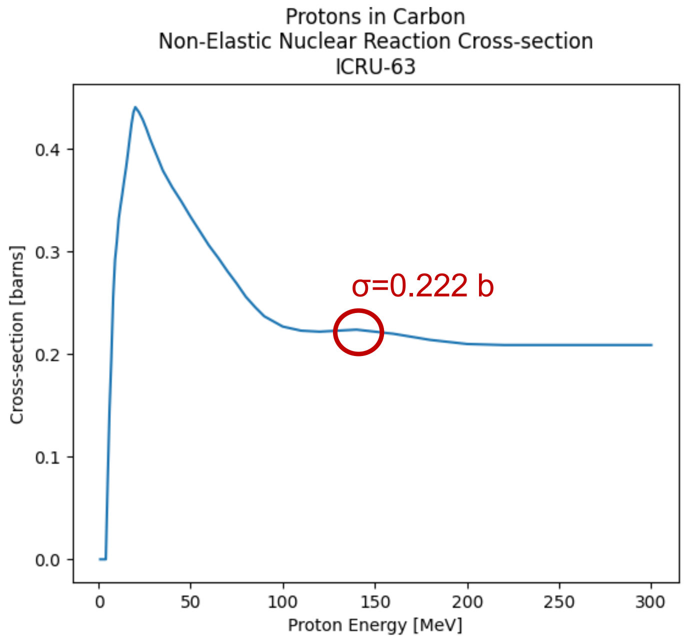


- ***G. Parisi, G. Schettino and F. Romano. 2022, Phys.Med.Biol.*** *https://doi.org/10.1088/1361-6560/ac79fb*
- **Relative uncertainty of $\bar{y}_D$** for increasing numbers of detected events
- $\bar{y}_D = \frac{1}{\bar{y}_F}\int_0^\infty y^2 f(y)dy$
- Strong impact of nuclear interaction events
- About $5 \cdot 10^7$ **events for** $u(\bar{y}_D) < 10\%$ in proton entrance region

Nuclear Interactions influence on $\bar{y}_D$ uncertainty

Fragment	E (MeV)	LET (keV/µm)	Range (µm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

Table 1 - Nuclear reaction products of 180MeV protons in water.
From: *Tommasino and Durante 2015*



- Much **lower E**
- Higher Z
- Very high LET → very high ***y***

- $\Sigma = \frac{N_A \rho}{M_{mol}} \sigma = \mathbf{3.9 \cdot 10^{-6} \mu m^{-1}}$
- Very low probability of occurrence
- $\sim 5 \cdot 10^{10}$ events to have 10^4 inelastic nuclear interaction.

Nuclear Interactions influence on $\bar{y}_D$ uncertainty

Results for different charged particles and different impinging energies

$\left[\frac{MeV}{u}\right]$	proton	He ion	C ion
250			
100			
55			
12			

Lower energy:
$y_{primary}$ closer to $y_{fragments}$

250 MeV proton 1μm diamond detector		250 $\frac{MeV}{u}$ carbon 1μm diamond detector	
$\bar{y}_D \left[\frac{keV}{\mu m}\right]$	$\sigma_{CS}(\bar{y}_D)$ $at\, 10^7\ counts$	$\bar{y}_D \left[\frac{keV}{\mu m}\right]$	$\sigma_{CS}(\bar{y}_D)$ $at\, 10^7\ counts$
45.45	*19.7%*	*64.52*	*6.4%*

Target fragments:
- $Z_{fragment} > 1$
- $y_{fragment} \gg y_{proton}$

Target & primary fragments:
- $Z_{fragment} \leq 6$ mainly
$y_{fragment} \sim > y_{carbon}$

Without NI	3.86	0.2%

NI-focus code features

Follow-up analysis: code upgrade

- Event ID (history #)
- Single event energy deposition
- Particle path length
- Particle Z

← Each detected event →

G4Step() -> GetTrack() -> GetCreatorProcess() -> GetProcessName();

IF generated by Nuclear Interaction

↓

Nuclear interaction event →

- Event ID (history #)
- Fragment Z
- Fragment A
- Deposited energy by the fragment
- Path length of the fragment
- Volume in which it was generated

➢ Contributions from each fragment:
  - Microdosimetry spectrum
  - Mean values
➢ Where are fragments generated? Breakthrough in the influence of detector structure
➢ Characterisation of fragments path length

NI-focus follow-up

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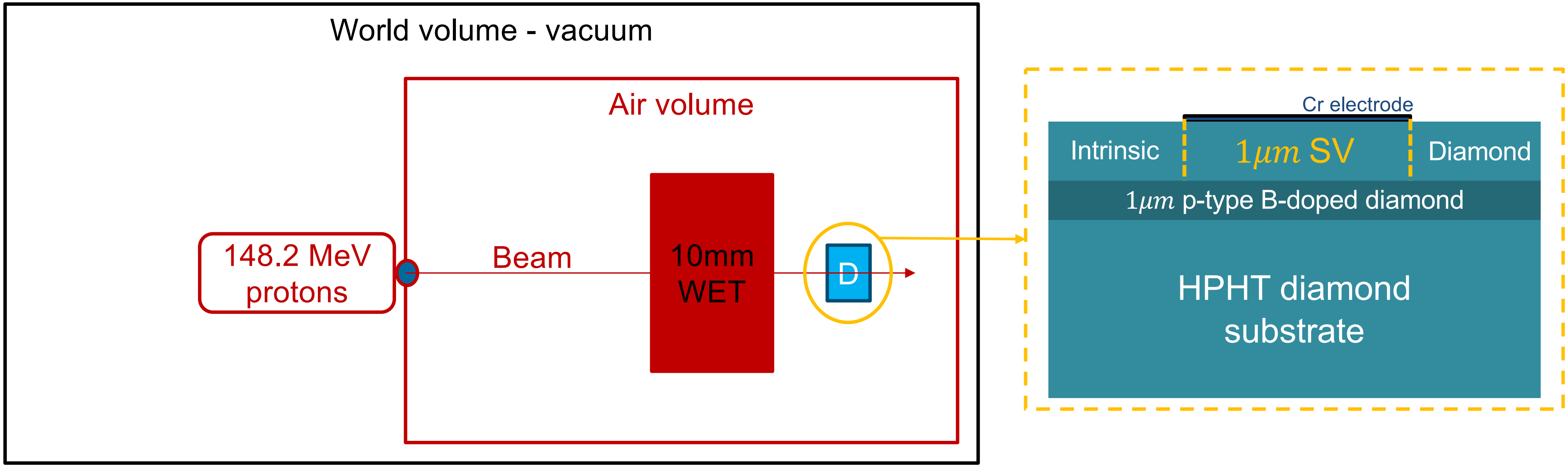
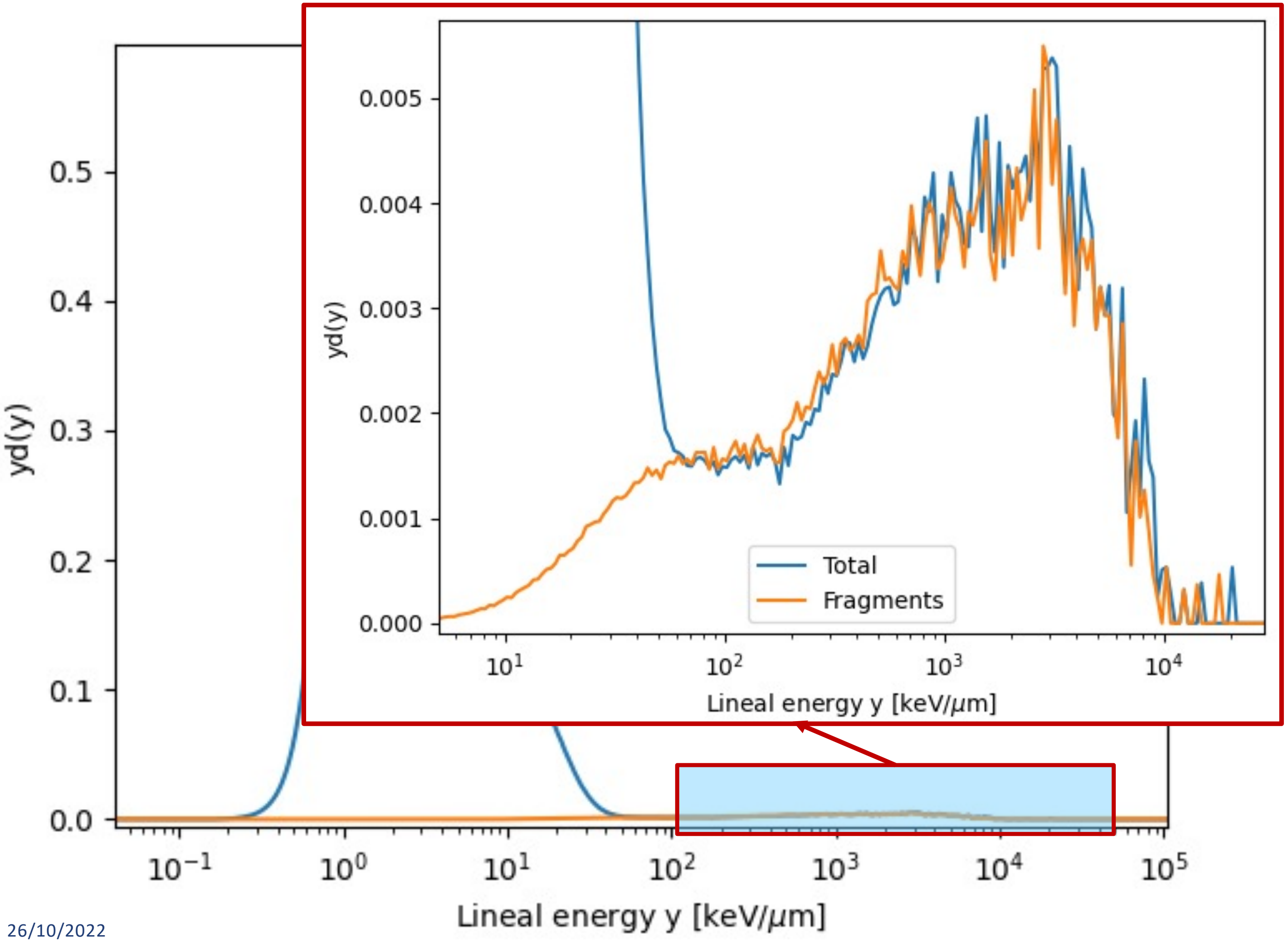
Simulation geometry and physics lists



Physics Lists:

- G4EmLivermorePhysics
- G4DecayPhysics
- *G4HadronElasticPhysicsHP*
- *G4HadronPhysicsQGSP_BIC_HP*
- *G4IonBinaryCascadePhysics*

The 148.2MeV proton microdosimetric spectrum



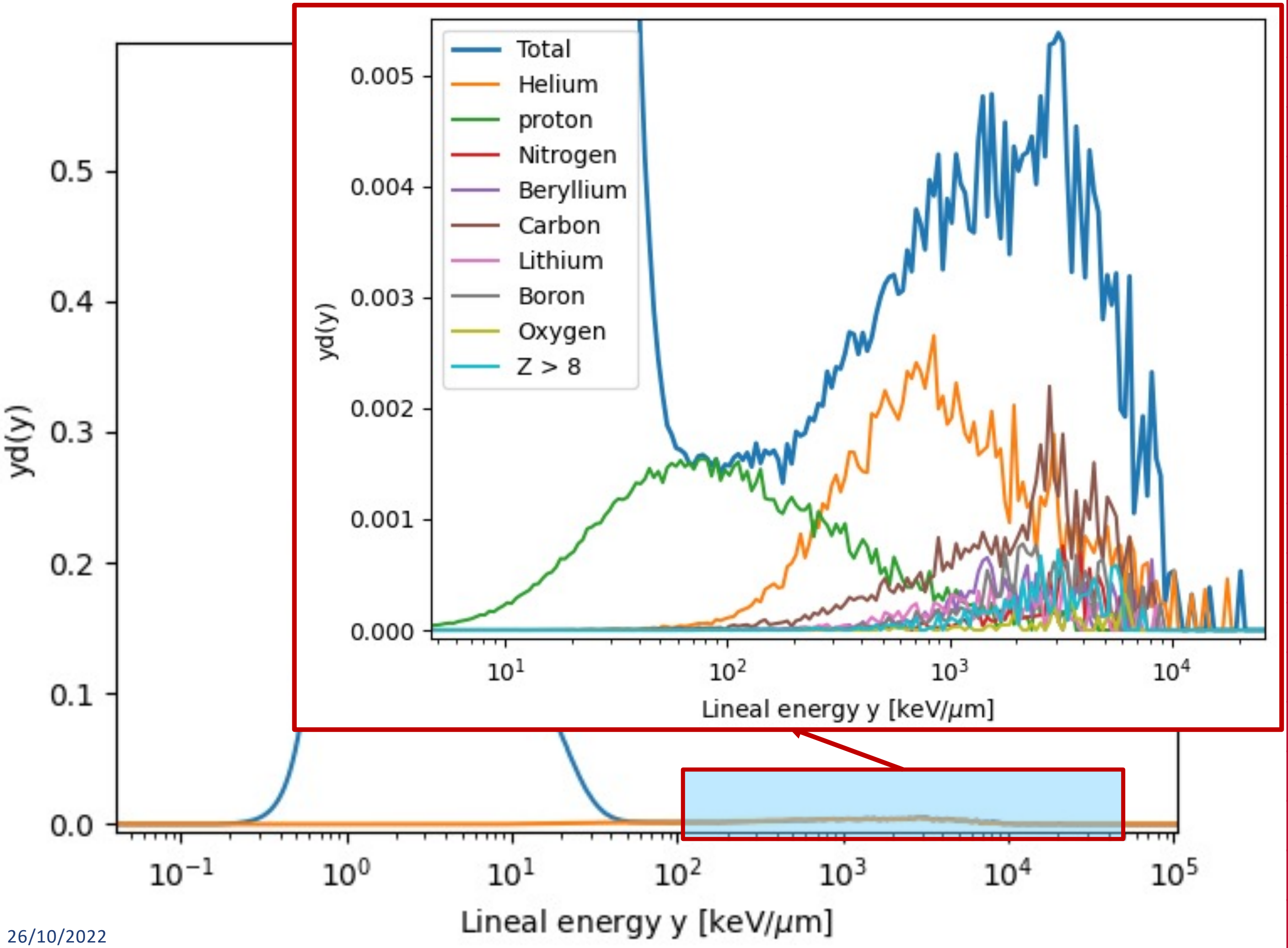
0.02% NI events

NI origin, process %:

- 98.15 % Inelastic
- 1.83 % Elastic
- 0.02% Coulomb scattering

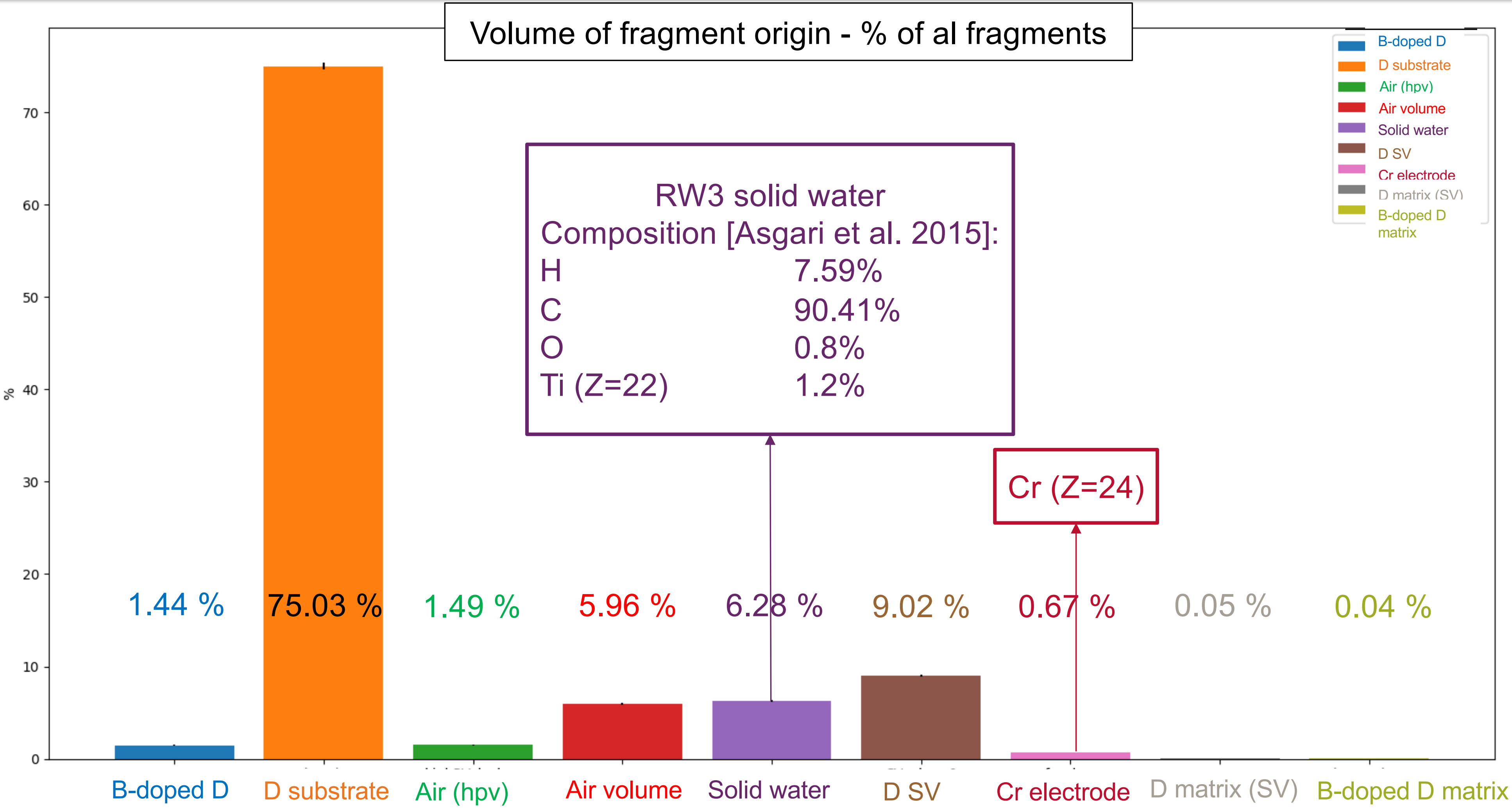
	$\bar{y}_F$	$\bar{y}_D$
"True" value	1.59 $\frac{keV}{\mu m}$	32.97 $\frac{keV}{\mu m}$
Contribution from NI	1.59 %	79.77 %
NI deactivated	1.57 $\frac{keV}{\mu m}$	6.78 $\frac{keV}{\mu m}$

NI-focus 148.2MeV proton



	Z	% of NI	% to $\bar{y}_F$	% to $\bar{y}_D$
H	1	**88.08**	0.47	3.9
He	2	8.08	**0.55**	**29.29**
Li	3	0.43	0.05	3.59
Be	4	0.44	0.07	5.83
B	5	0.42	0.09	7.47
C	6	2.05	0.25	**19.58**
N	7	0.19	0.04	4.48
O	8	0.06	0.01	1.5
F	9	< 0.01	< 0.01	0.03
Cl	17	< 0.01	< 0.01	0.04
Ar	18	< 0.01	< 0.01	0.2
K	19	0.01	< 0.01	0.28
Ca	20	0.01	< 0.01	0.32
Sc	21	0.02	0.01	0.96
Ti	22	0.06	0.02	1.42
V	23	0.08	0.02	1.37
Cr	24	0.05	0.01	0.46
Mn	25	0.01	< 0.01	0.04

NI-focus 148.2MeV proton: where are fragments originated?



Conclusion summary

Nuclear interactions

Often overlooked

Huge impact on $\bar{y}_D$

Huge impact on $\bar{y}_D$ uncertainty

Potential significance in radiobiological outcomes

Experimentally hard to detect and characterise

Long computational times

Big uncertainties of cross-section data

References

G. Parisi et al., "*Microdosimetry for hadron therapy: a state of the art of detection technology*",* in: ***Frontiers in Physics, 2022

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Thank you

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