Microdosimetry for proton treatment planning

Jacopo Magini (University of Surrey)

Pietro Pisciotta (University Medical Center Groningen)

Erik Traneus (RaySearch Laboratories)

Mohammad Hussein (National Physics Laboratory)

Agnes Angerud (RaySearch Laboratories)

Francesco Romano (INFN)

Giuseppe Schettino (University of Surrey)

Microdosimetric Kinetic Model

- based on time evolution equation for lethal and potentially lethal lesions
- can be applied to experimental data
- requires x-ray data
- gives a linear relation between average microdosimetric value and survival curve

$$S(D) = \exp - \left(\left(\alpha_0 + \frac{\beta}{\rho \, \pi \, r_d{}^2} y^* \right) D + \beta D^2 \right)$$

RBE can be obtained from S(D)
but not the other way around

How to score MKM values?

Geant4:

+ widely validated for microdosimetry and clinical application
+ can score individual electrons' energy deposit with an arbitrary accuracy
- modelling a specific patient is *very* difficult
- illegal to use for treatment planning

Raystation:

+ easy patient modelling from CT scan
+ very fast proton, neutron, and alpha transport
- proton energy deposit modelled via tabulated stopping power
- spatial resolution $\gtrsim$ mm

NOTE: microdosimetric spectra are scored in $\gtrsim\mu$m volumes, and the energy is deposited by electrons, not the primary beam

Best compromise:

- simulate transport via Raystation and get some macroscopic value for a specific voxel

- apply look-up tables made via Geant4 that associate the previous value to a microdosimetric mean

What macroscopic value?

- kinetic energy spectrum per voxel
  - usually enough to univocally identify a spectrum
  - both Geant4 and Raystation can score it

- LUT: primary kinetic energy → microdosimetric means
  - various monochromatic beams are simulated separately in Geant4
  - for each beam a spectrum is obtained, and from it the corresponding y^*
  - thus each mono beam is associated to a y^*

- put the two together!
  - for each bin of a kinetic energy spectrum, find the corresponding y^* from the LUT
  - average those y^* over the whole spectrum, with the bins' heights as weights

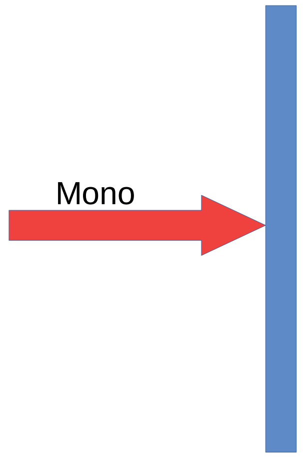
- … and the resulting y^* gives the MKM RBE
  - or can be combined with other radiobiological models

LUT production

1/2: simulation setup

- monochromatic proton beams on a 1µm slab
  - their kinetic energies are picked in a log range
  - proton are shot directly into the water slab
  - spectra are collected
  - … and from them the kinetic energy → y^* LUT populated
  - while we're at it, we also collect the other means $(\bar{y}_F, \bar{y}_D)$

- repeat the procedure for neutron beams
  - but not for heavier hadrons (more on this later)



This and the following Geant4 setups are based on the Radioprotection advanced example

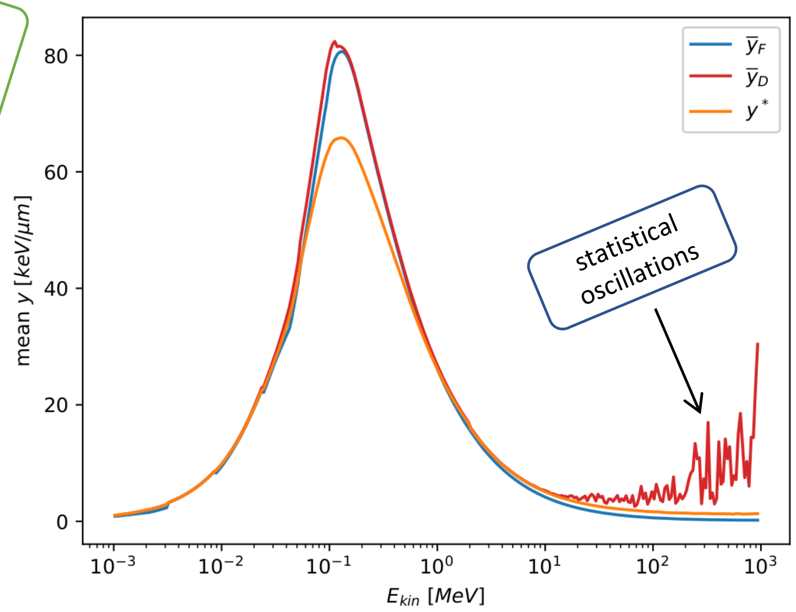
LUT production

2/2: resulting LUT

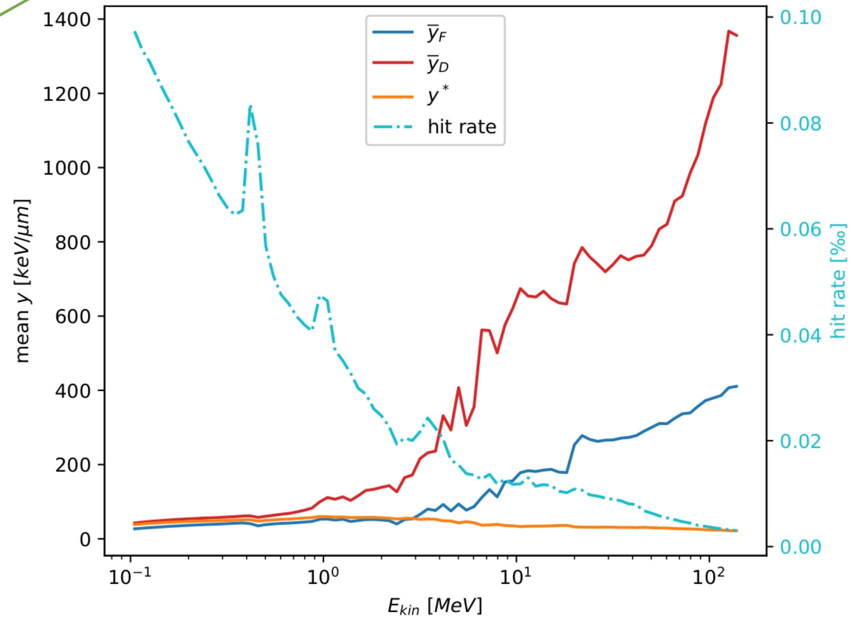
- results are shown on the right
  - LUT for all microdosimetric means
  - only y^* is really needed for the MKM
- are neutrons really relevant?
  - their means in the LUT are *extremely* high

    but
  - their interaction rate is very low
- let’s apply these LUT to a simple test setup

Protons LUT



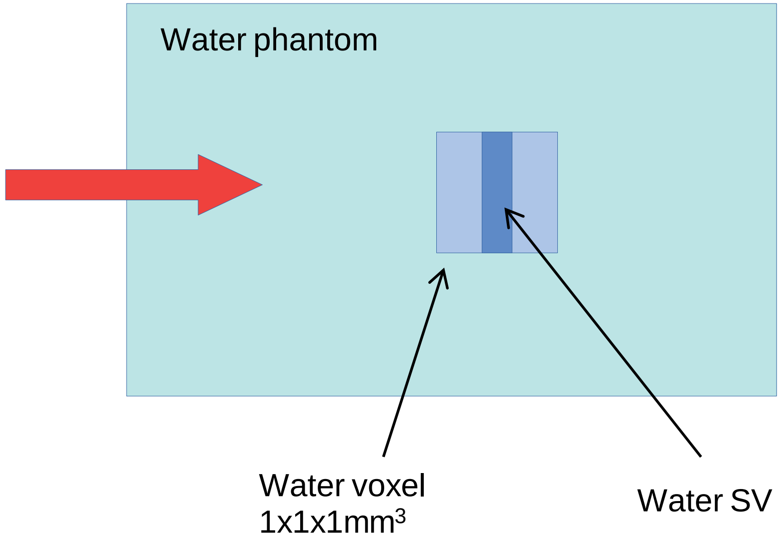
Neutrons LUT



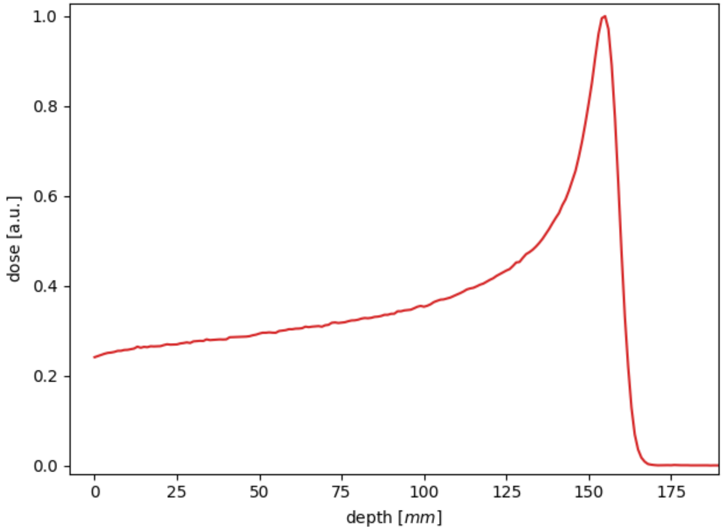
Preliminary tests

1/2: a simple test setup

Not to scale



- build a TPS-like setup in Geant4
  - place a 1mm voxel inside a water phantom
  - at several depths throughout a 150MeV Bragg curve
    (σ=1.5MeV spread)
- place a SV inside each pixel
  - 1μm width, placed in the middle of the pixel
  - it scores the microdosimetric spectrum "the normal way"
    i.e. it gives a microdosimetric that can be used later as a reference
  - kinetic energies of protons and neutrons are scored when they enter this SV
    we apply the LUT to the resulting kinetic energy spectra
- let's see what the resulting kinetic energy spectra look like!



Preliminary tests

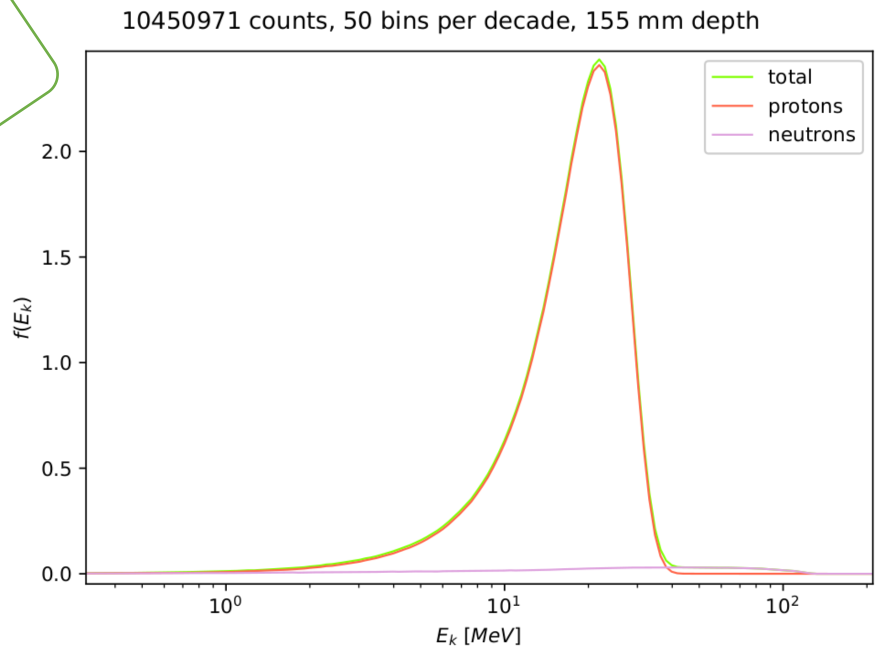
2/2: results

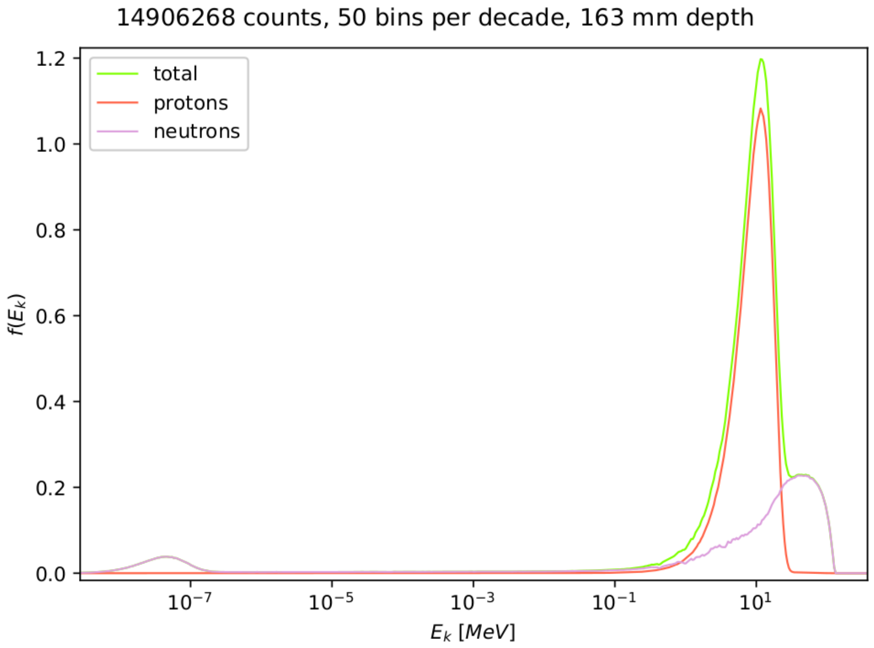
Kinetic energy spectra shown for two depths in water

- resulting kinetic energy spectra
  - mostly composed of protons
  - neutrons are also present, and build up with depth
  - almost no particle with $Z > 1$

<u>however</u>

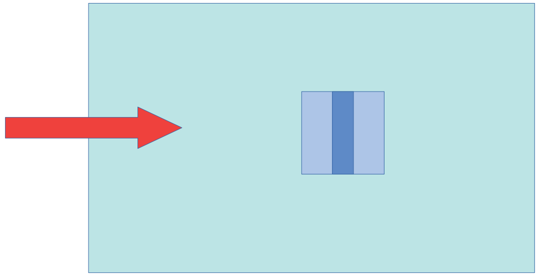
- *inside* the SV high Z events are recorded
  - they cause energy deposits with large y
  - very short path length: they are rarely seen *entering* the SV, so don't contribute to the kinetic energy spectrum
  - … but since their whole existence is confined within the SV, the LUT will include them "for free"!
- now we have some test spectra for the LUT…
  - a set of kinetic energy spectra to which the LUT can be applied
  - a set of microdosimetric spetra, to test whether the resulting y^* are accurate





LUT application

1/2: how to average the kinetic spectrum



- let’s apply the LUT to the test setup
  - if it works, the same LUT can be used for other, more complex setups
- applied to each pixel’s kinetic energy spectrum
  - the LUT means are averaged, with the kinetic energy spectrum as weight
  - the weighting is done by taking each mean’s definition and replacing its quantities with the ones in the LUT:

Microdosimetric mean from LUT, obtained from a mono beam with energy E_i

Height of the bin centred in E_i in the kinetic energy spectrum

$$\bar{y}_F = \int y \cdot f(y)\,dy \rightarrow \sum_i \bar{y}_{F\,LUT}(E_i) \cdot f(E_i)$$

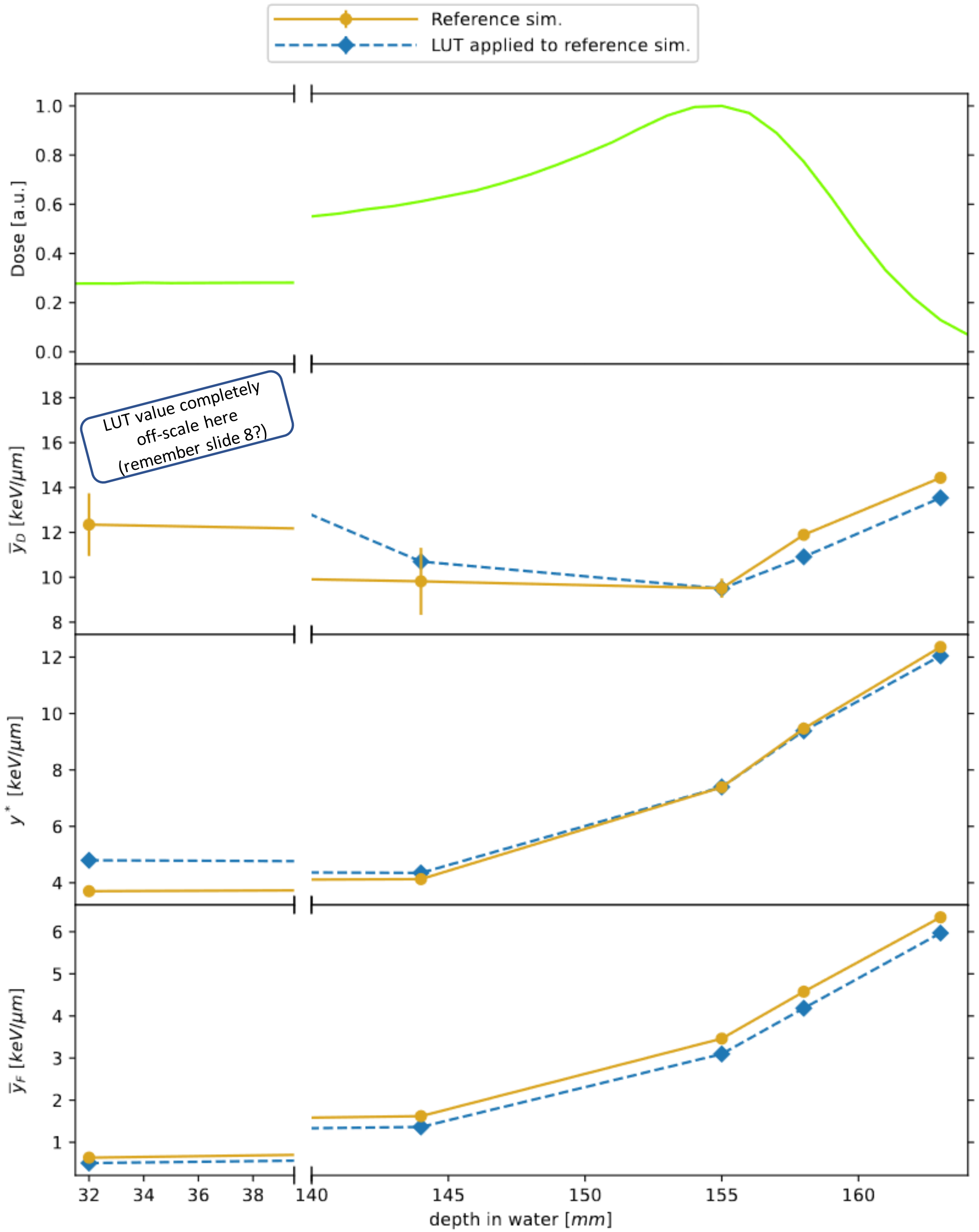
$$\bar{y}_D = \frac{1}{\bar{y}_F}\int y^2 \cdot f(y)\,dy \rightarrow \frac{1}{\bar{y}_F}\sum_i \left(\bar{y}_{D\,LUT}(E_i)\right)^2 \cdot f(E_i)$$

$$y^* = \frac{{y_0}^2}{\bar{y}_F}\int \left(1-\exp(-y^2/{y_0}^2)\right)\cdot f(y)\,dy \rightarrow \frac{{y_0}^2}{\bar{y}_F}\sum_i \left(1-\exp(-{y^*_{LUT}}^2/{y_0}^2)\right)\cdot f(E_i)$$

LUT application

2/2: comparison with reference values

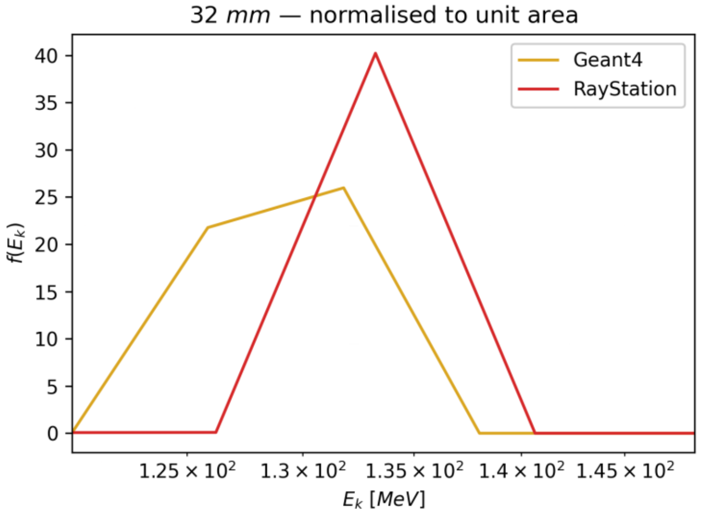
- the means obtained can be compared with those of the reference spectrum
  - the ones that were obtained from the SV in the reference simulation
- excellent agreement
  - ... between reference simulation and LUT approach (almost) everywhere
  - the former, accurate approach requires a cut $\lesssim$ 1µm
  - ... while the latter doesn't require any electron tracking at all!
- we can now move onto Raystation

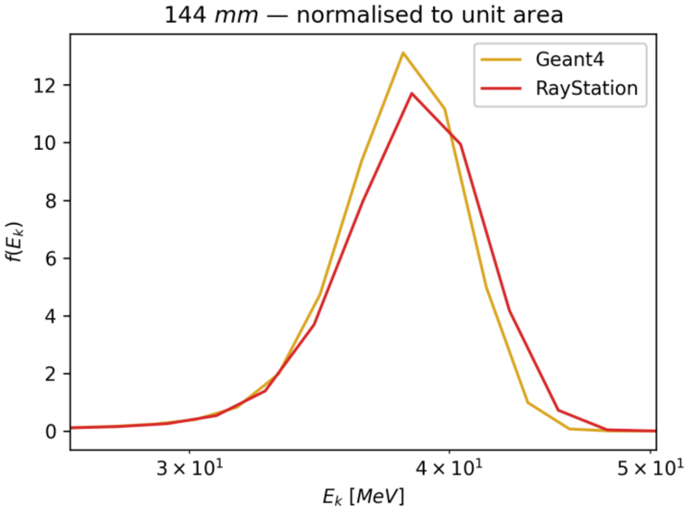


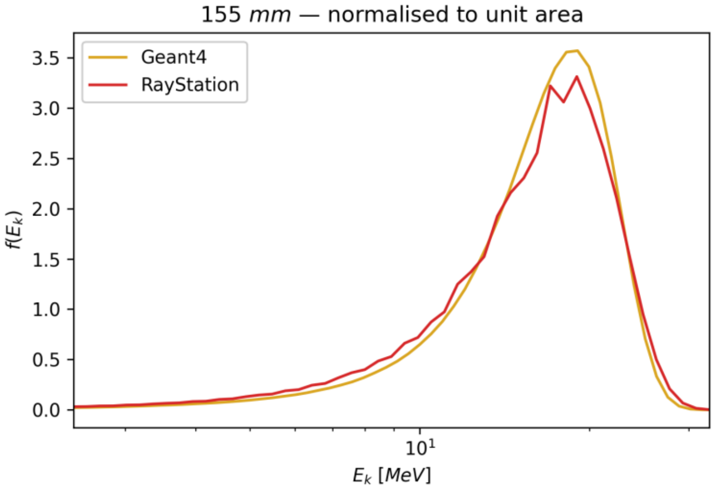
Raystation

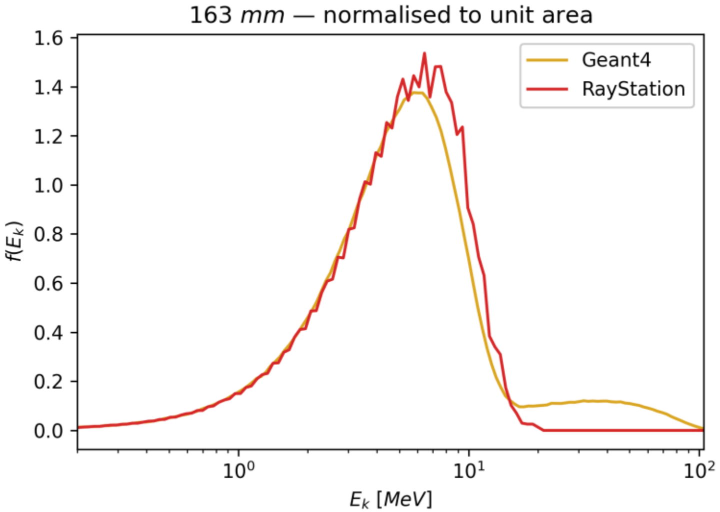
1/2: preliminary tests

- can we reproduce the test setup in Raystation?
  - even simpler setup: no beam spread
  - resulting kinetic spectra are very similar
  - best agreements at intermediate depths
  - discrepancies at very low/high depths
- let’s apply the LUT
  - ... and see how these discrepancies affect the results





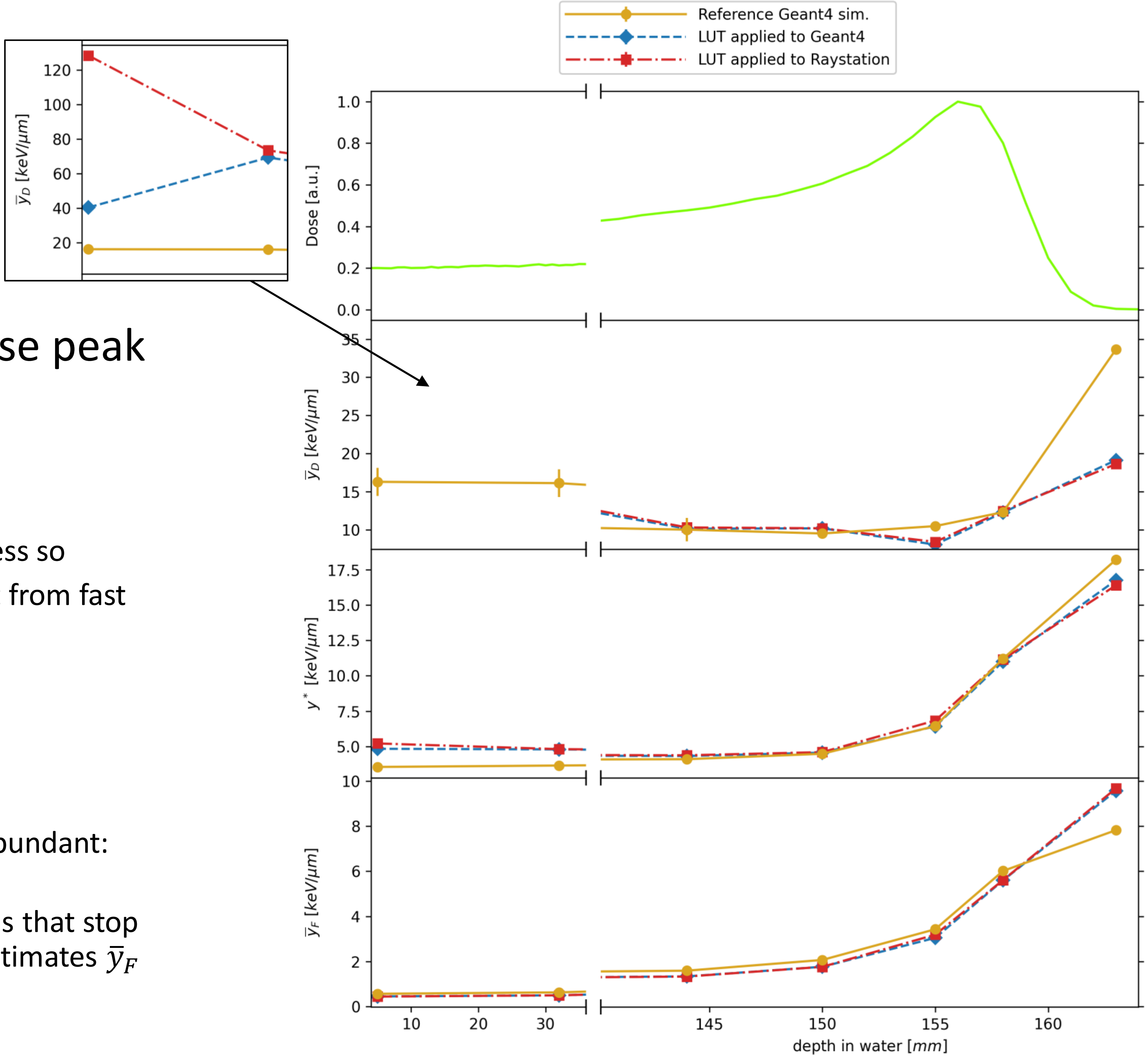




Raystation

2/2: preliminary results

- good agreement around dose peak
  - regardless of mean
- issues at low depths
  - $\bar{y}_D$ is massively overestimated, y^* less so
  - LUT struggle with high energy event from fast protons
- issues at very high depths
  - few protons reach this far
  - neutrons become more relatively abundant: ignoring them underestimates $\bar{y}_D$
  - a lot of events are caused by protons that stop *before* the SV: ignoring them overestimates $\bar{y}_F$



Next steps

in order or priority

- improve LUT for fast protons
  - in the entrance $\bar{y}_D$ is strongly overestimated, and y^* slightly
  - the LUT have trouble dealing with rare high energy events caused by fast protons
  - more statistics? Clever fitting of LUT at high energies?

- reduce discrepancies at high depths
  - include neutron (and higher Z?) LUT in test setup
  - modify LUT production setup to account for electron-only events

- test more complex geometries in Raystation
  - e.g. CT scans of patient

- apply to pre-existing clinical data
  - where treatment planning was carried out with Raystation
  - can we map NTC to hotspot of microdosimetric means?

完

the end

Backup slides

Raystation

3/2: preliminary results [extended]

- issues at very high depths
  - few protons reach this far
  - neutrons become more relatively abundant: ignoring them underestimates $\bar{y}_D$
    - they cause very high energy events which could explain why $\bar{y}_D$ in the reference simulation is that much higher
  - a lot of events are caused by protons that stop *before* the SV: ignoring them overestimates $\bar{y}_F$
    - usually their contribution is small, since this kind of events is infrequent
    - just after the maximum range of the primary protons they become much more relevant!
    - they *should* be low energy events, which reduce the value of $\bar{y}_F$ but have limited effect on $\bar{y}_D$