RĪGAS TEHNISKĀ UNIVERSITĀTE

1862

Physical and biological property comparisons of ^{4}He and ^{3}He ion beams for applicability in radiation therapy

Kristaps Paļskis (RTU, CERN)

Under the supervision of prof. Toms Torims (RTU)
Maurizio Vretenar (CERN)
prof. Joao Seco (DKFZ)
Mariusz Sapinski (PSI, SEEIIST)

RĪGAS TEHNISKĀ UNIVERSITĀTE

Background: **Helium ions for particle therapy**

- Proving intermediate physical and biological characteristics between protons and carbon ions, **helium ion therapy is returning to «novelty horizon»**
- Clinically – helium-4 ion beams are mainly considered

There is another stable helium isotope to consider for ion therapy: **Helium-3**

RĪGAS TEHNISKĀ UNIVERSITĀTE

Background:
In favour of helium-3

Helium-3 ions provide favourable characteristics from accelerator physics point-of-view due to

their charge-to-mass ratio of 2/3 compared to ½ of ^{4}He:

Beam rigidity

For the same maximum range of 30 cm in water:

for ^{3}He: **260 MeV/u**

for ^{4}He: **220 MeV/u**

Corresponding magnetic rigidity:

for ^{3}He: **3.74 T*m**

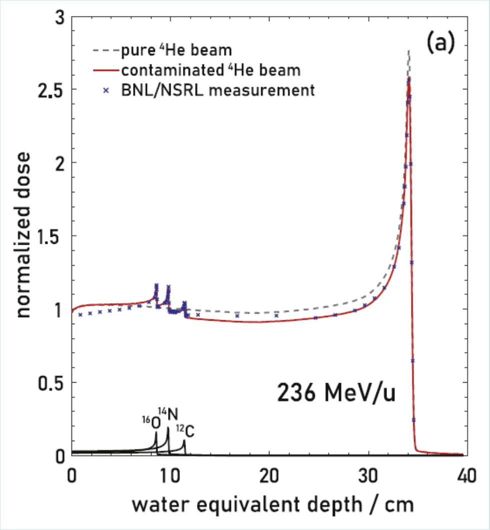
for ^{4}He: **4.52 T*m**

Same magnetic field – 1.2 lower ring radius

Contamination at injection

For ^{4}He, other ion species with q/m = ½ from the plasma source can contaminate the beam at injection

(^{12}C, ^{14}N, ^{16}O)



Background:
Clinically relevant physics of ^{3}He

With the rationale from favourable accelerator performance with the use of ^{3}He beams, question is

How do ^{3}He ion beam differs from ^{4}He ion beam parameters in relevant physical and biological aspects for a clinical use?

The aim of this work

Linear Energy Transfer distributions

Physical dose:
Depth dose and lateral profiles

Neutron fluence and **kinetic energy distributions**

Within a simulation framework, **compare ^{3}He and ^{4}He ion** beams, extracting relevant physical and biological parameters for clinical use

Biological dose:
RBE distributions

The aim of this work

Linear Energy Transfer distributions

Physical dose:
Depth dose and lateral profiles

Neutron fluence and **kinetic energy distributions**

Within a simulation framework, **compare ^{3}He and ^{4}He ion** beams, extracting relevant physical and biological parameters for clinical use

Positron emitter distributions

Biological dose:
RBE distributions

Prompt gamma emissions

Methodology
Main simulation parameters

- Geant4 simulation framework for **unperturbed beams** (*no initial energy spread and contamination)*
  - 10^6 particles in **water** – dose distribution parameter estimation
  - 10^7 particles in **skeletal muscle tissue** – positron emitter and prompt gamma yield estimation
- Initial energies for range of 100–150 mm **in water**
  - **129.8 to 180.1 MeV/u for ^{3}He**
  - **109.3 to 151.3 MeV/u for ^{4}He**
- Physical quantities scored:
  - Energy deposition and LET by particle type
  - Kinetic energy by particle type
  - Neutron fluence and kinetic energy
  - Positron emitter isotope yields and spatial distributions
  - Vertex data of prompt gamma emissions + corresponding process and parent particles

Methodology
Main calculational aspects

Physical dose distribution calculations

- Physical dose based spread-out Bragg peak optimization
(*superposition of pristine Bragg peaks*)

Relative Biological Effectiveness calculations, biologically driven optimization

- Relative Biological Effectiveness calculation with Microdosimetric Kinetic model
- Biologically driven spread-out Bragg peak optimization

Positron emitters signal estimation

- Yield distribution conversion into integrated activity
- Positron range considerations for activity distribution

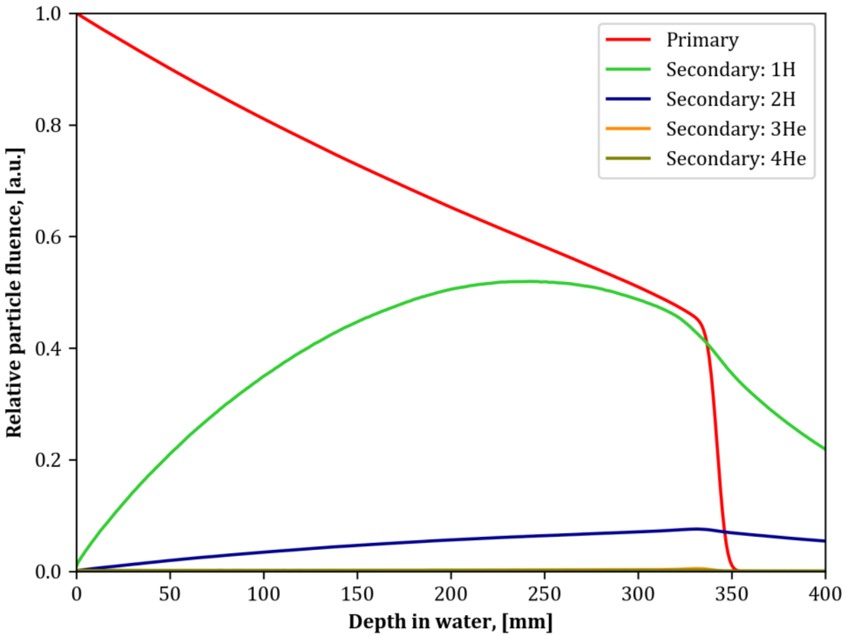
Prompt gamma signal estimation

- Prompt gamma energy spectrum and emmision depth distribution
- Prompt gamma spectrum separation by physical interaction processes

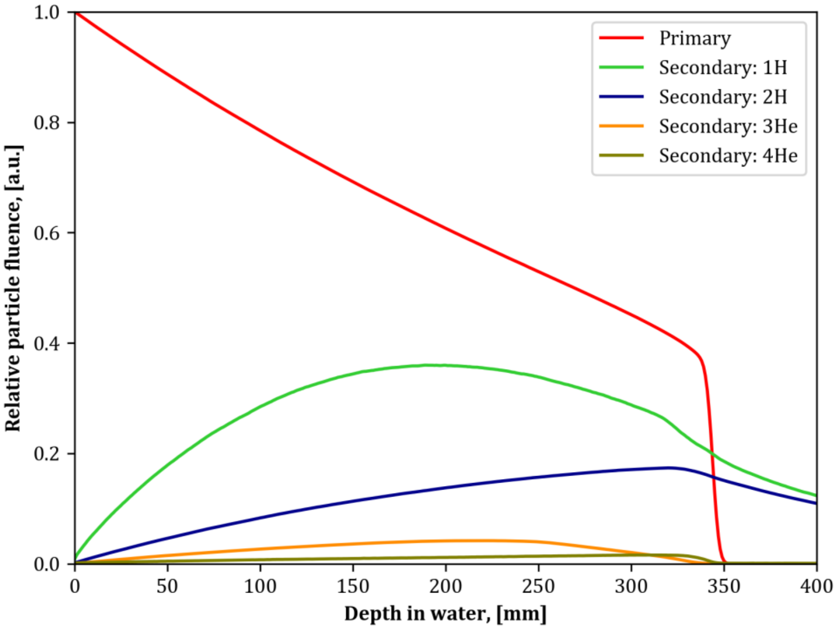
RĪGAS TEHNISKĀ UNIVERSITĀTE

Results
Constituents of the *mixed beam*

Undergoing matter interactions, particle beam is *mixed* – primary helium ions and various secondaries (*projectile fragmentation and target fragmentation*)

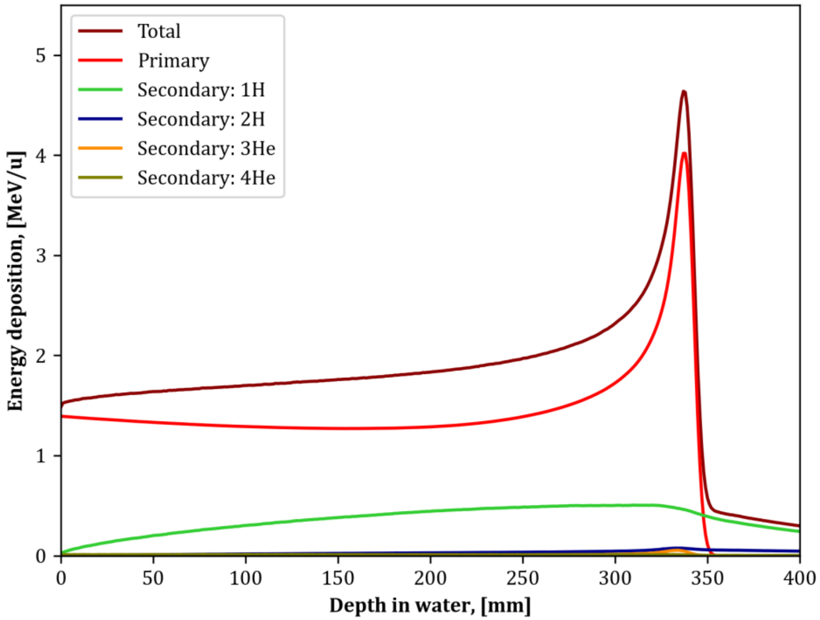


Particle fluences of main constituents of **^{3}He beam**
(r = 35cm, E = 278.2 MeV/u)

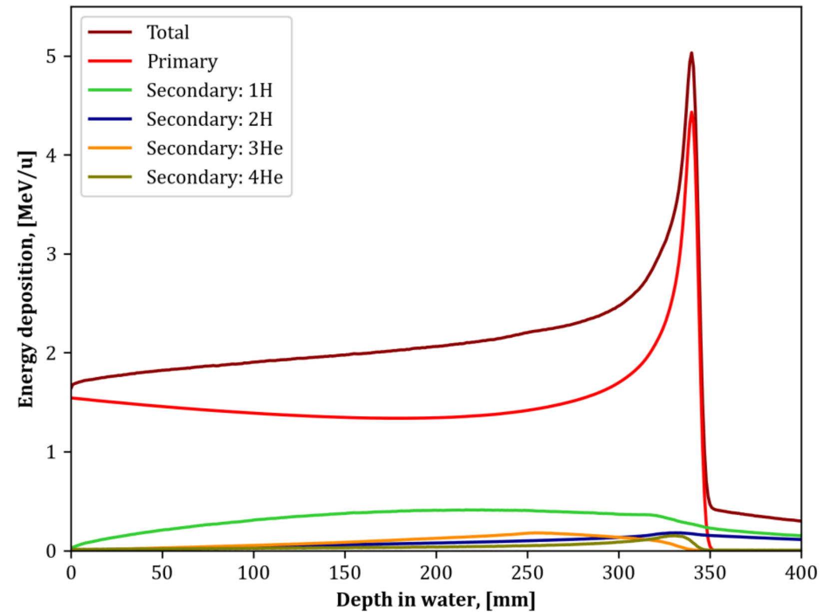


Particle fluences of main constituents of **^{4}He beam**
(r = 35cm, E = 234 MeV/u)

Results
Constituents of the *mixed beam*



Energy deposition of main constituents of ^{3}He beam
(r = 35cm, E = 278.2 MeV/u)

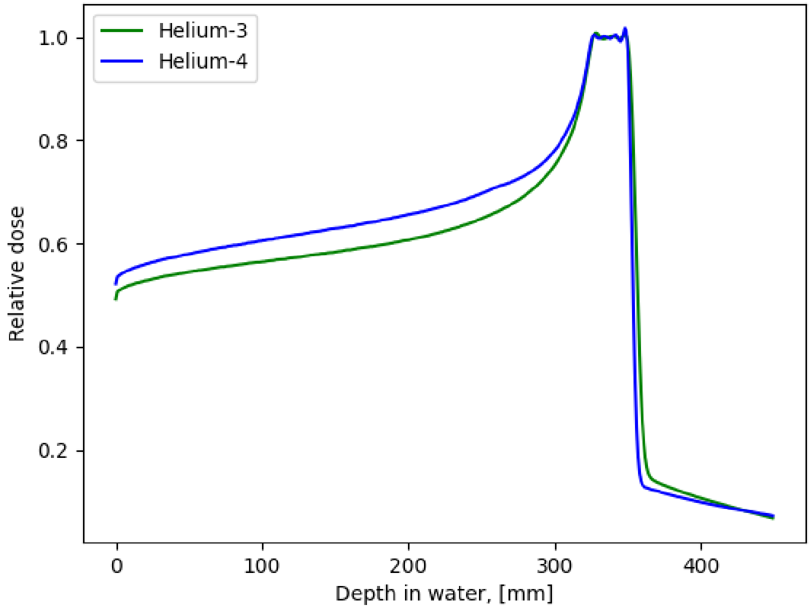


Energy deposition of main constituents of ^{4}He beam
(r = 35cm, E = 234 MeV/u)

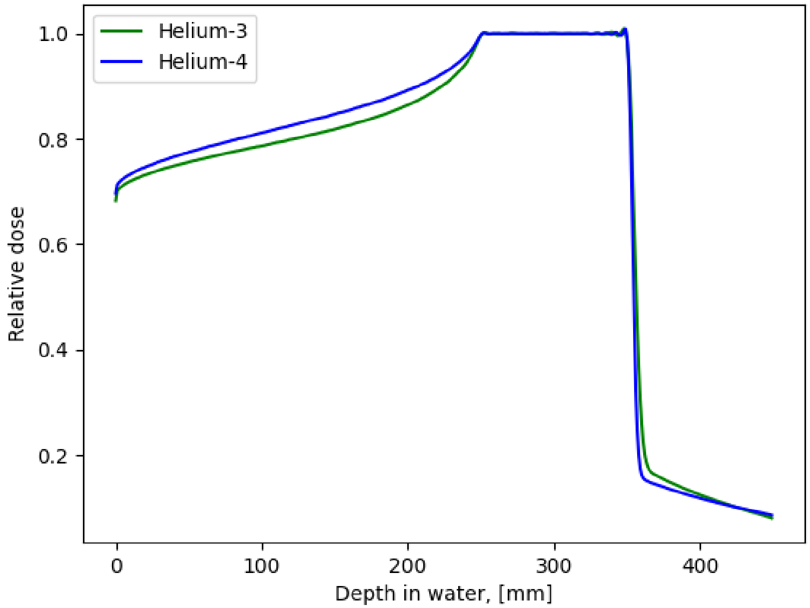
^{4}He ion beams *undergo* more nuclear reactions, resulting in steeper decrease of primary fluence and higher contributions of secondary fragments

Results
Physical SOBPs: IDD approach

IDD – integrated depth dose, radially integrated all deposition contributions



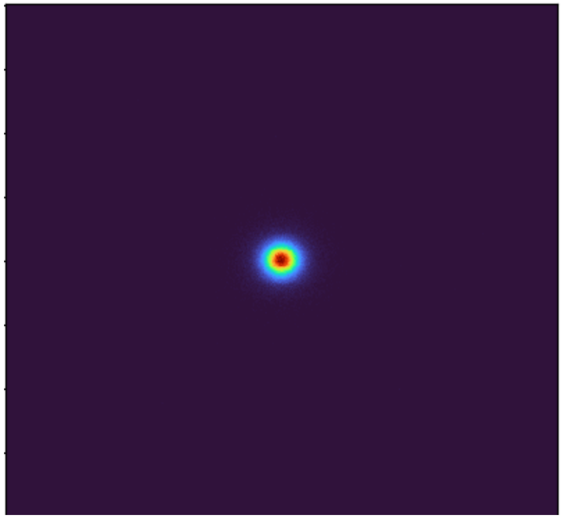
Physically optimized SOBP:
25 mm length, distal end at 350 mm



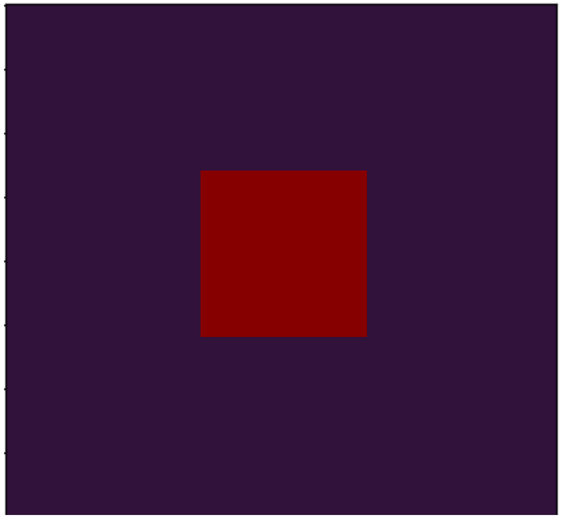
Physically optimized SOBP:
100 mm length, distal end at 350 mm

^{3}He beams – lower entrance dose (*up to 5%*)
exhibits more at large depths and smaller tumors

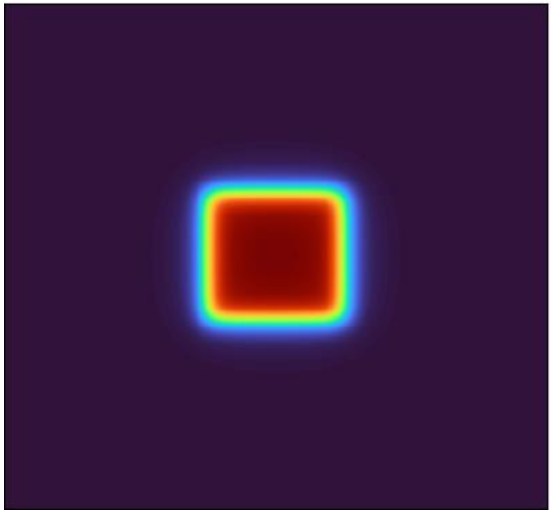
Results
Physical SOBPs: PB convolution



X



=



Energy deposition pencil beam (kernel)

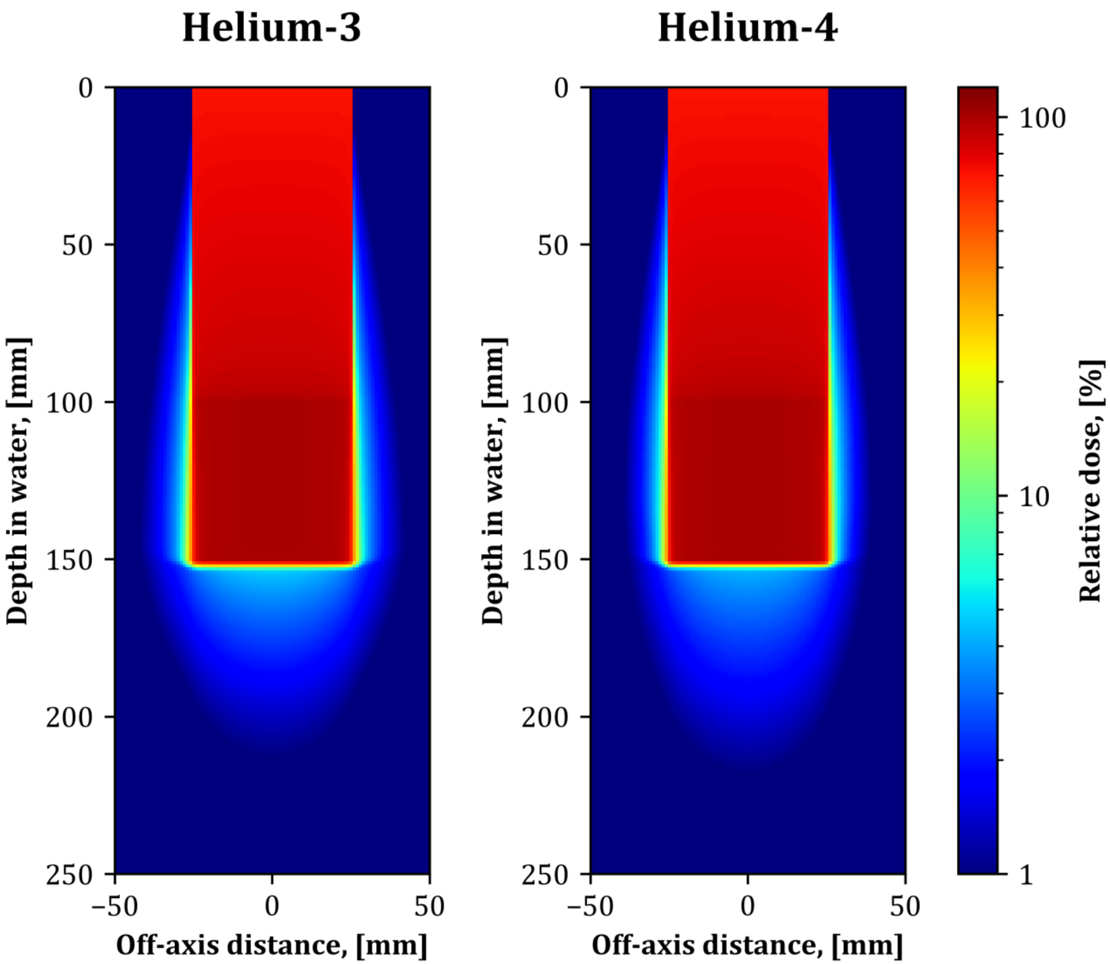
Fluence map (*radiation field*)

Dose distribution corresponding to a particular radiation field

RĪGAS TEHNISKĀ UNIVERSITĀTE

Results
Physical SOBPs: 2.5D distribution

Dose distribution map for a simulated **5x5x5** tumor at 15 cm distal depth (*left* – ^{3}He ions, *right* – ^{4}He ions)



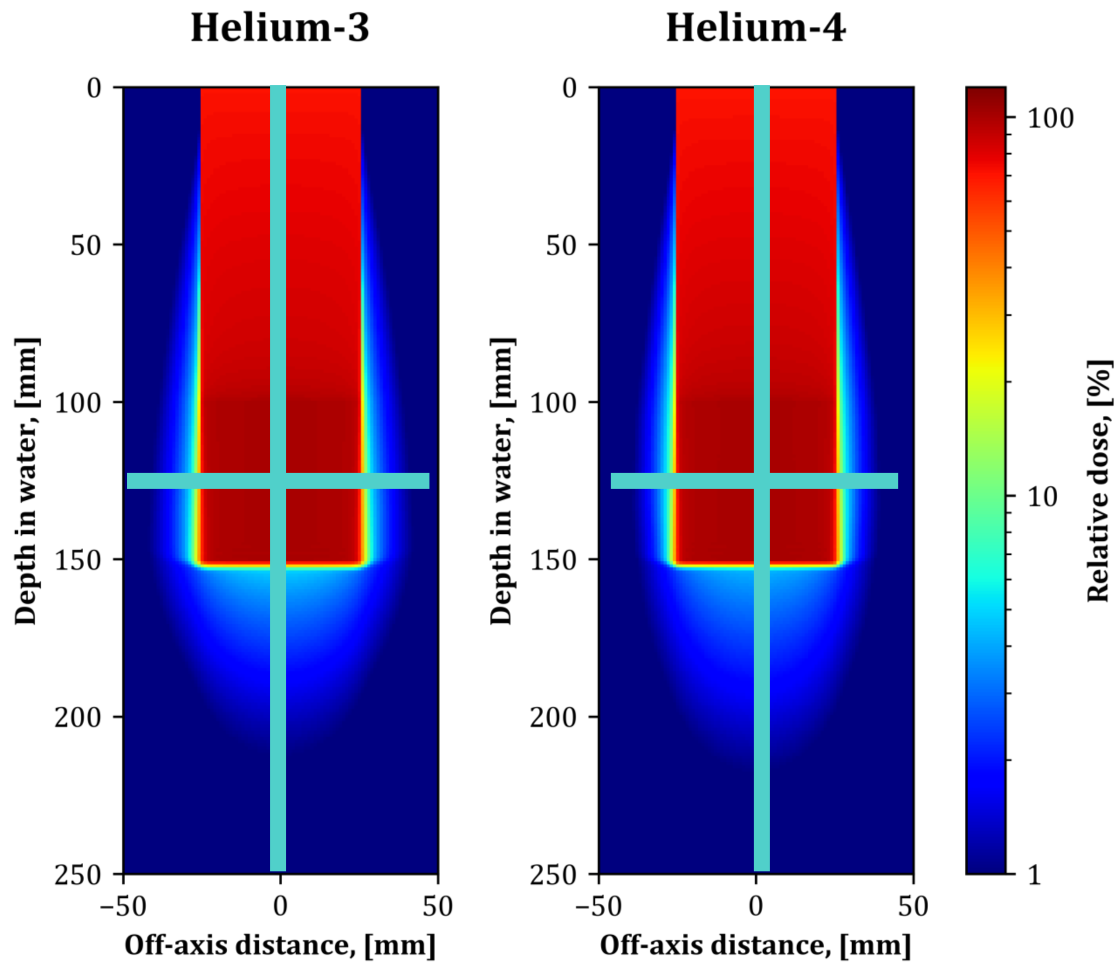
^{3}He beams exhibit broader lateral distribution due to scattering.
Fragmentation tail narrower, more «forward-peaked» for 4He ion beams

1862
RĪGAS TEHNISKĀ UNIVERSITĀTE

Results
Physical SOBPs: 2.5D distribution

Dose distribution map for a simulated **5x5x5** tumor at 15 cm distal depth (*left* – ^{3}He ions, *right* – ^{4}He ions)

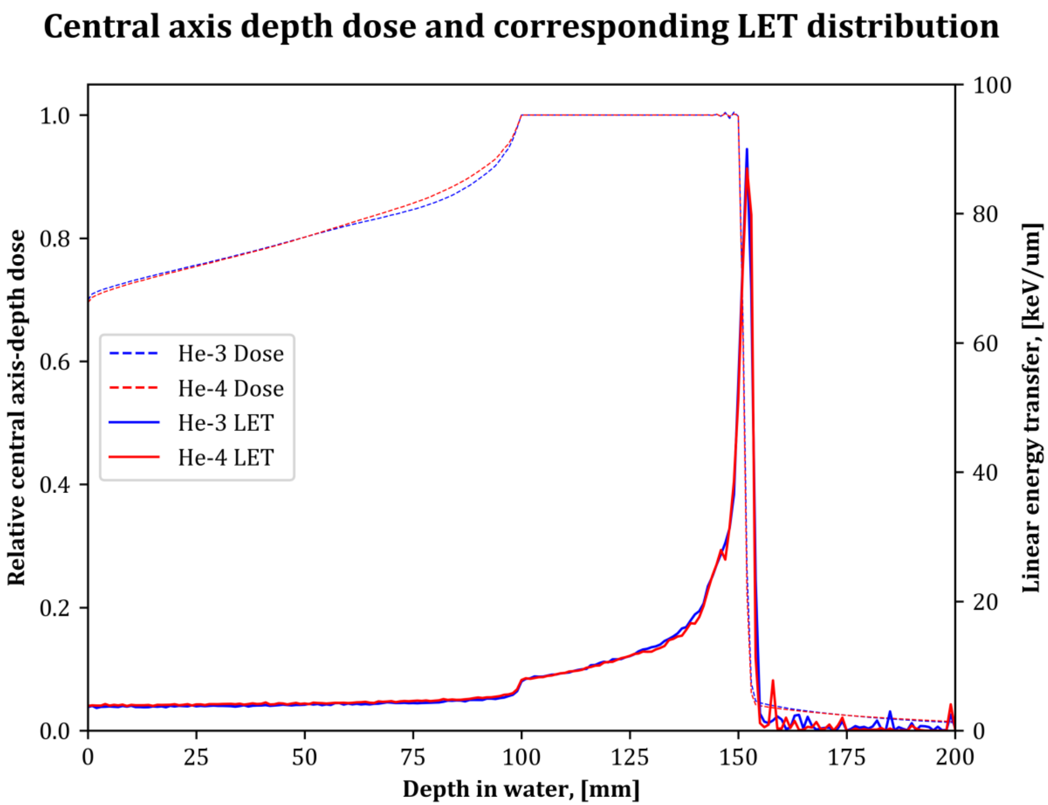
^{3}He beams exhibit broader lateral distribution due to scattering.
Fragmentation tail narrower, more «forward-peaked» for 4He ion beams



Results
Central axis depth dose and LET

^{3}He beams exhibit lower central axis entrance dose

Linear energy transfer values are comparable,
<u>BUT</u>
<u>heavily affected by initial beam conditions (realistic beam)</u>
(typically – higher for ^{4}He)

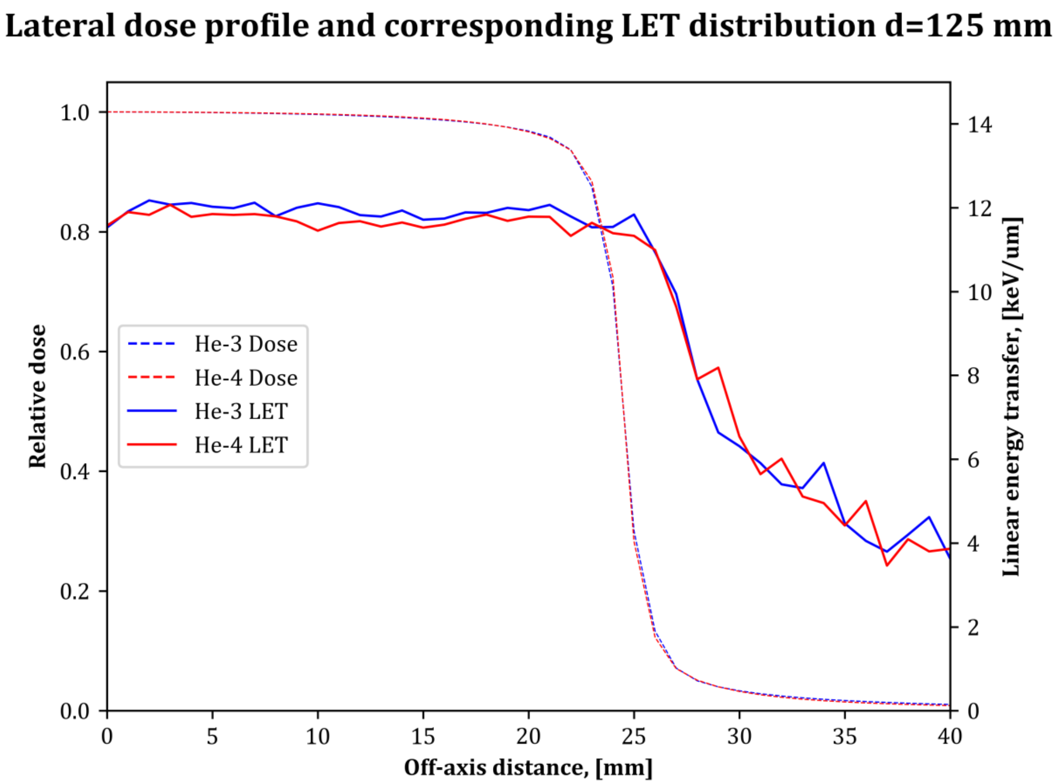


Central axis depth distribution and corresponding LET distribution comparison for a simulated 5x5x5 tumor irradiation

Results
Lateral profiles and LET

^{4}He beams exhibit *sharper* dose profile, comparing penumbras (*80%-20% dose level)* calculated
at 125mm depth:
for ^{3}He beam: **2.7 mm**
for ^{4}He beam: **2.4 mm**

Linear energy transfer values are comparable,



Lateral dose profile and corresponding LET distribution comparison for a simulated 5x5x5 tumor irradiation

RĪGAS TEHNISKĀ UNIVERSITĀTE

Results
Relative biological effectiveness

RBE – ratio of physical dose levels needed to deliver same cellular survival level for a particular radiation type compared to reference radiation (conventional gamma photons)

Kinetic energy distributions by particle type, weighed by deposited energy

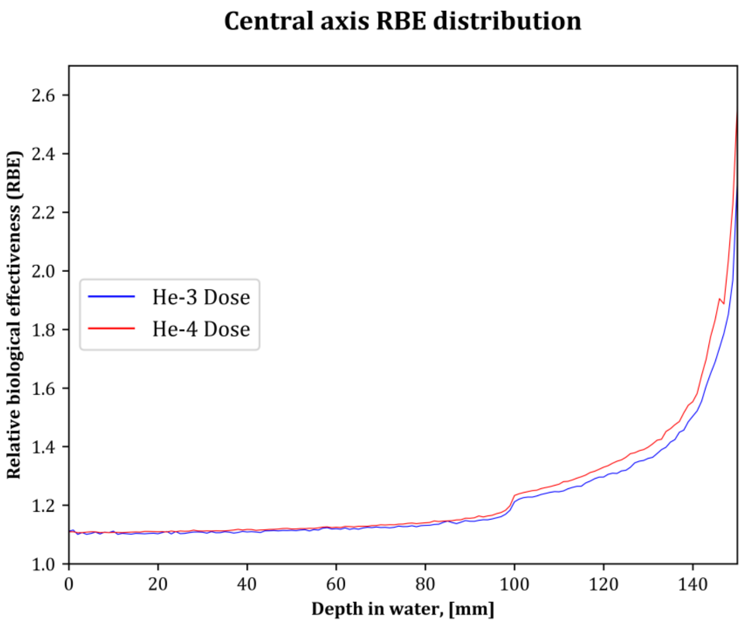
→

Kinetic energy distribution into dose-mean specific energy (*track structure model*)

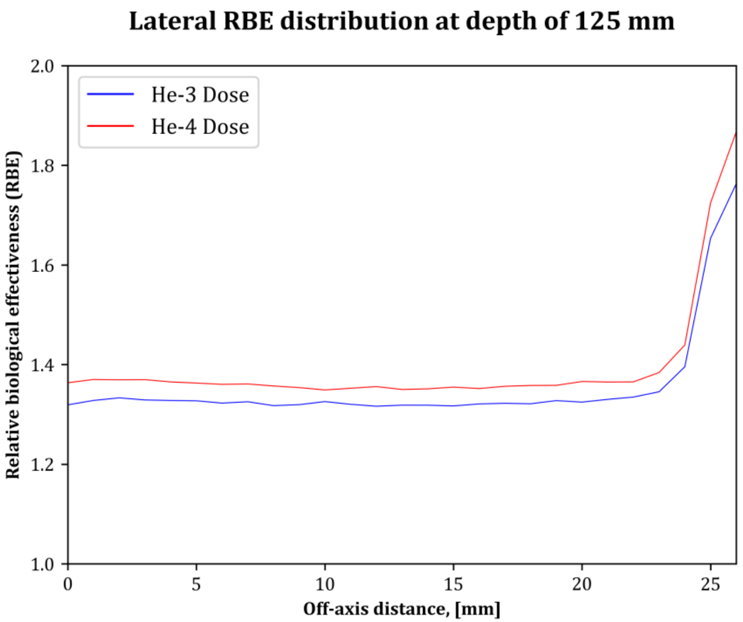
→

RBE value by Microdosimetric Kinetic Model, using HSG cell line parameters (*most common*)

Results
Relative biological effectiveness



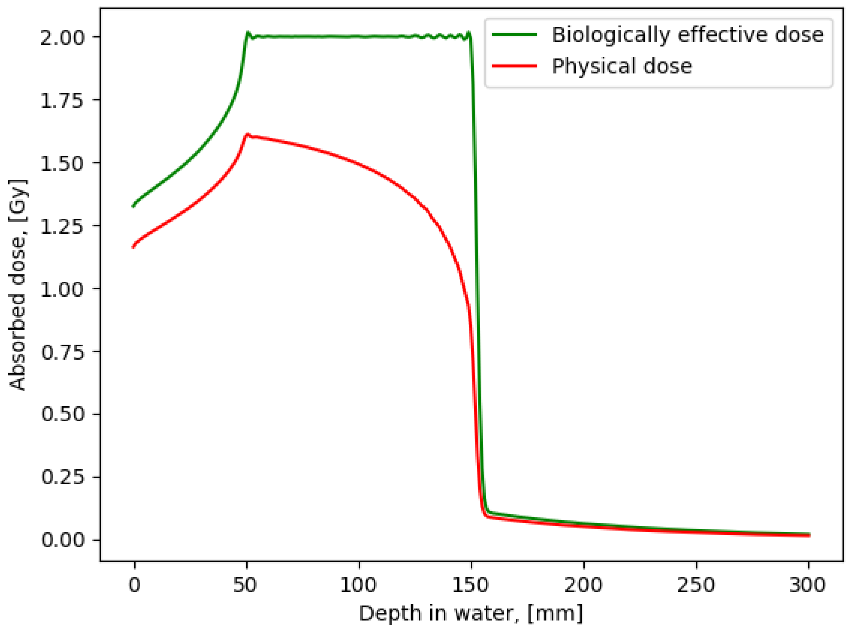
Central axis RBE distribution for a simulated 5x5x5 tumor irradiation



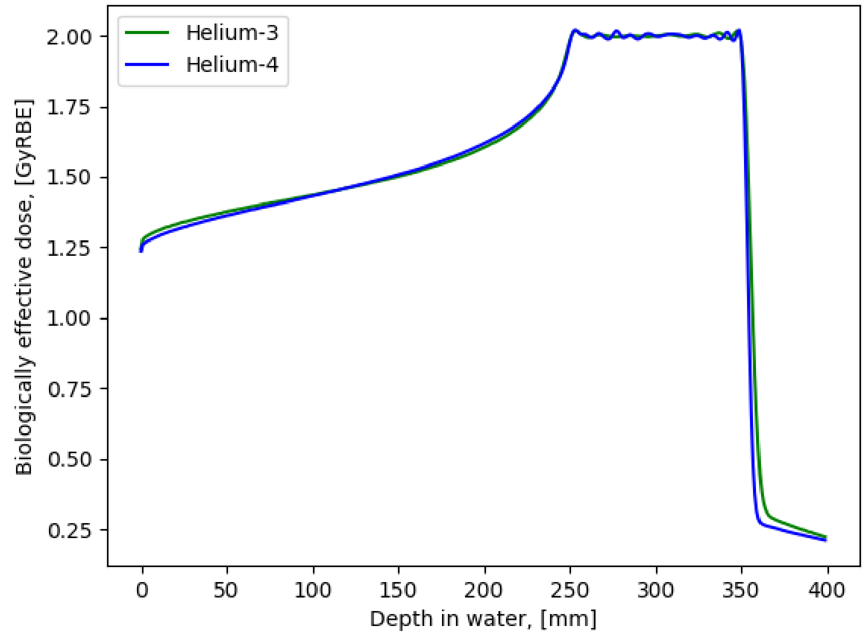
Lateral profile RBE distribution at 125 mm for a simulated 5x5x5 tumor irradiation

^{4}He beams exhibit comparable RBE in entrance channel, while ~ 5% larger RBE in SOBP region

Results
Biologically driven optimization



Biologically optimized SOBP: physical and biologically effective dose distributions



Biologically optimized SOBP comparison for ^{3}He and ^{4}He beams

Biologically optimized dose distributions show negligible level of differences

Results
Treatment range verification

Ions – main advantage

Ions *stop,* delivering a Bragg peak

Ions – main challenge

Ions *stop… **where is the Bragg peak?***

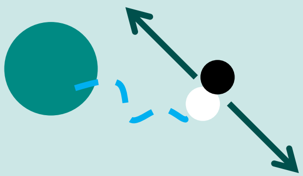
A priori – dual energy CT, ion radiography

On-line – **range verification**

Two main methods

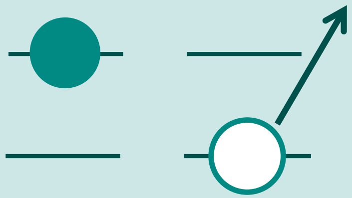
POSITRON EMITTERS

Nuclear reactions resulting in positron emitting nuclei, registration of the annihilation gammas (PET)

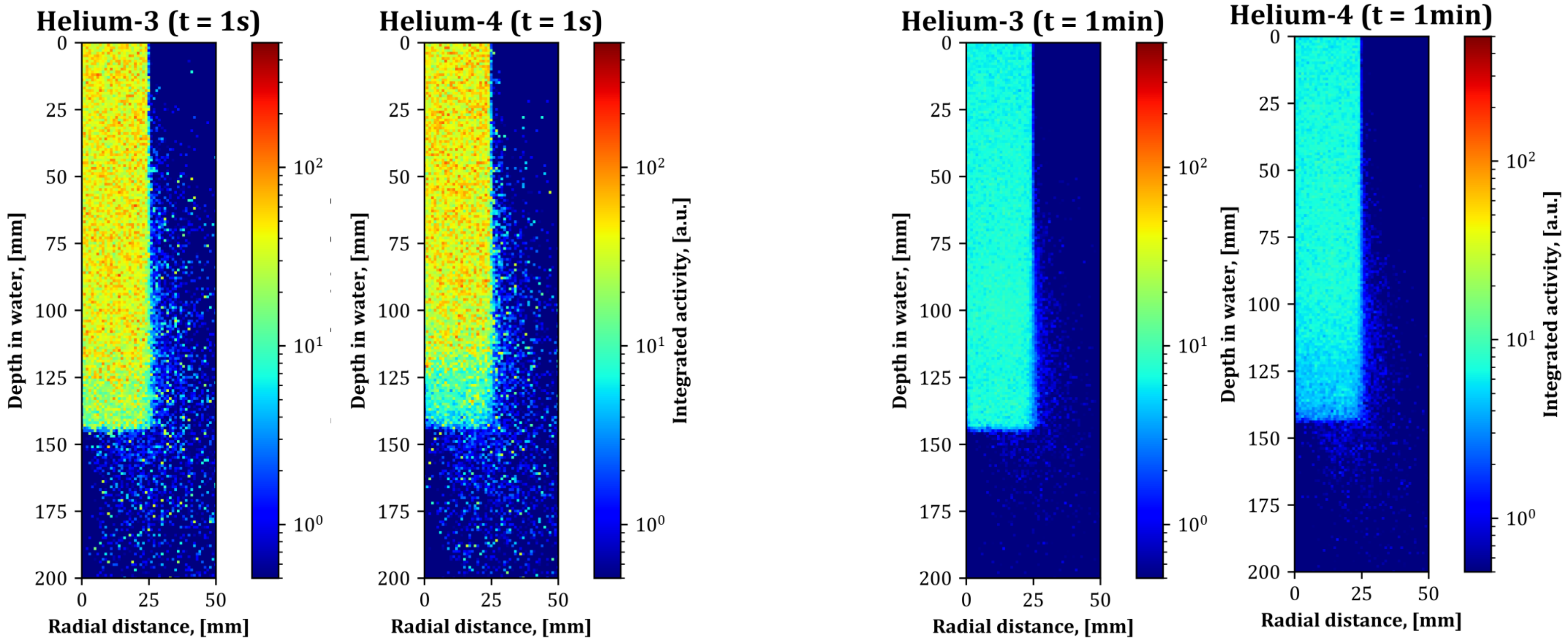


PROMPT GAMMAS

Nuclear reactions resulting in nuclei in excited states that relax by gamma emissions in ps range



Results
Positron emitter distributions



Integrated over 1 second

Integrated over 1 minute

RĪGAS TEHNISKĀ UNIVERSITĀTE

Results
Positron emitter distributions

^{3}He ion beams exhibit 5 – 10 % higher positron emitter production yields per incident particle

^{3}He ion beams exhibit lesser signal fall-off at distal end of the Bragg peak, owing to better correlation with dose distribution – **important factor for range verification**

Main signal components
Long lived

Positron emitter	$T_{1/2}$
^{15}O	122 s
^{13}N	9.97 min
^{11}C	20.34 min

Main signal components
Short lived

Positron emitter	$T_{1/2}$
^{12}N	11 ms
^{8}B	772 ms

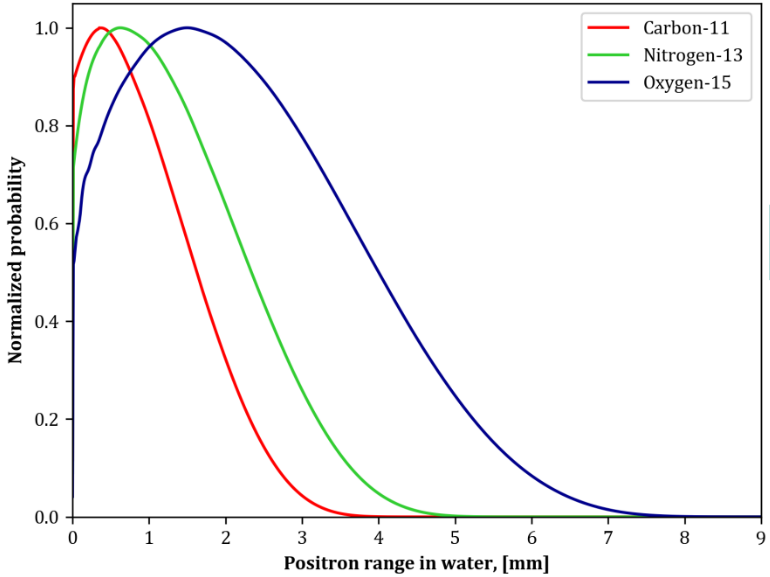
Results

«To do»: ADF introduction

Radioactivity map – emission of positrons **Positrons have range in a material**

ADF

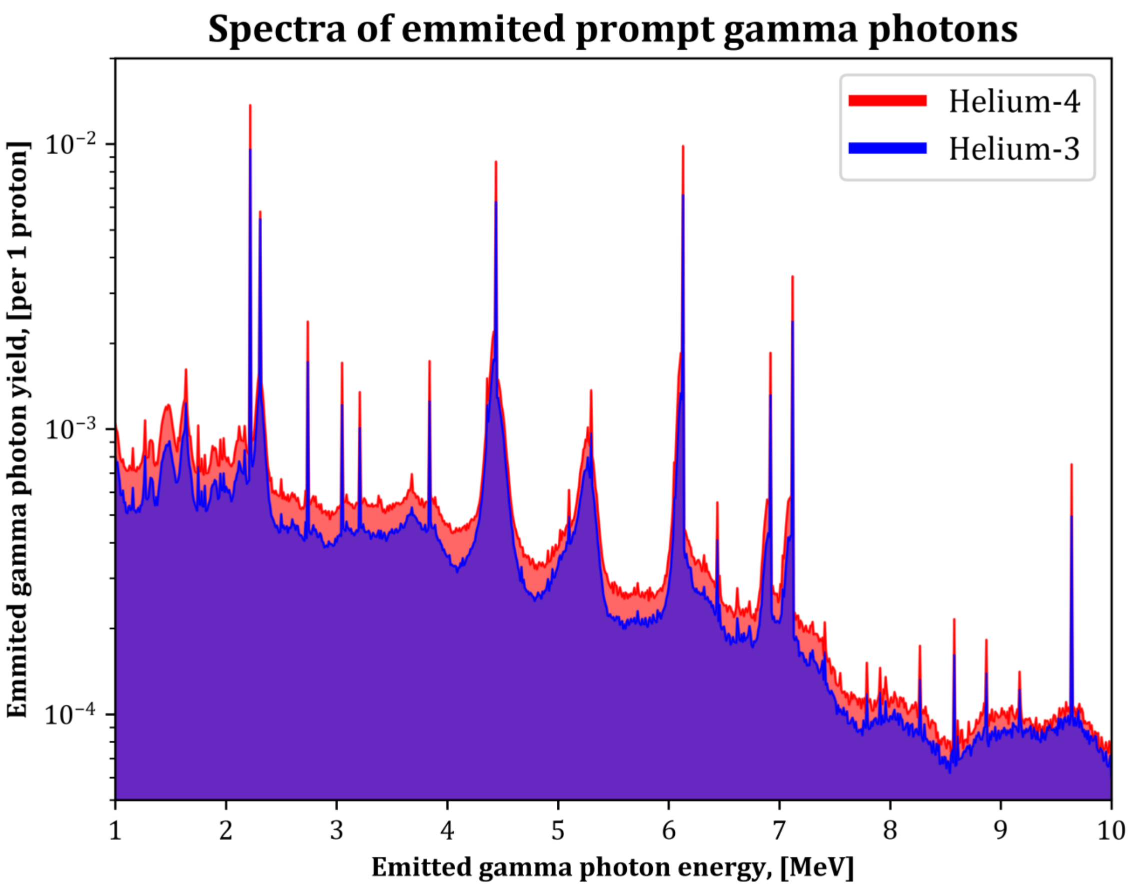
Positron annihilation vertexes – **Signal obtainable by PET**



Convolution kernels to use with radioactivity map – **obtainable annihilation signal**

RĪGAS TEHNISKĀ UNIVERSITĀTE

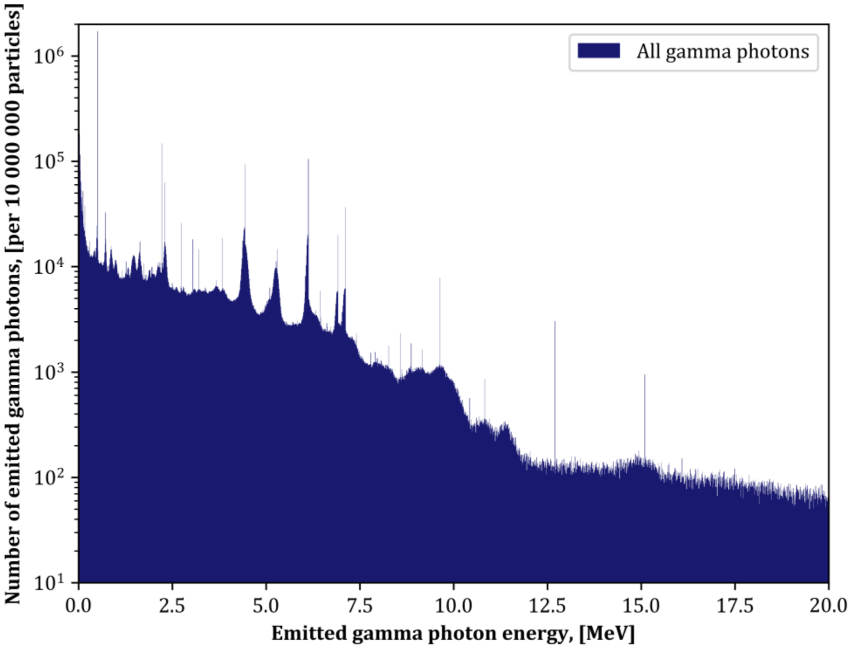
Results
Prompt gamma emission spectrum



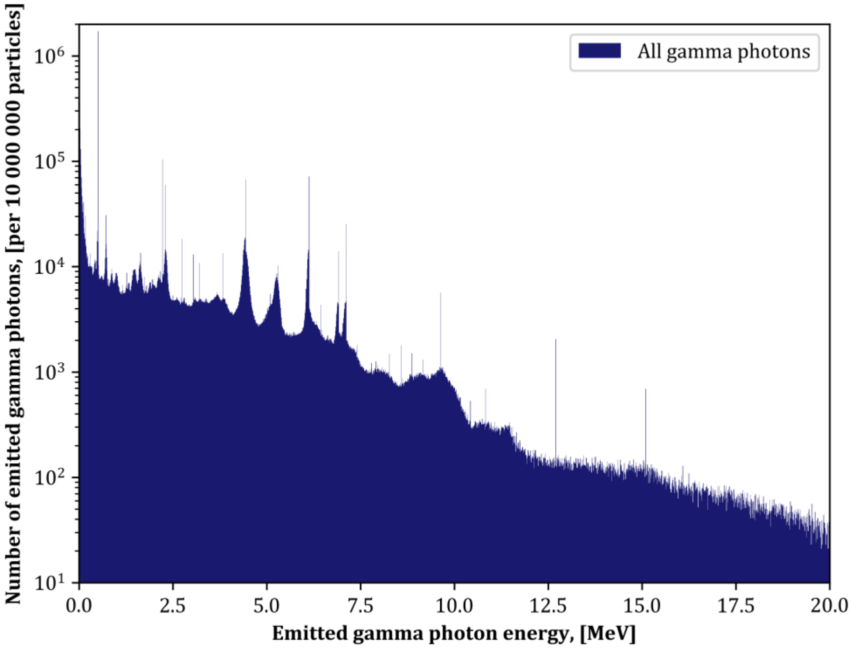
Prompt gamma emission spectrum for pristine Bragg peaks of ^{3}He and ^{4}He ion beams corresponding to 15 cm range

^{4}He ion beams exhibit higher production yields of prompta gammas – **around 1.2 – 1.3 times higher**

Results
Spectrum components

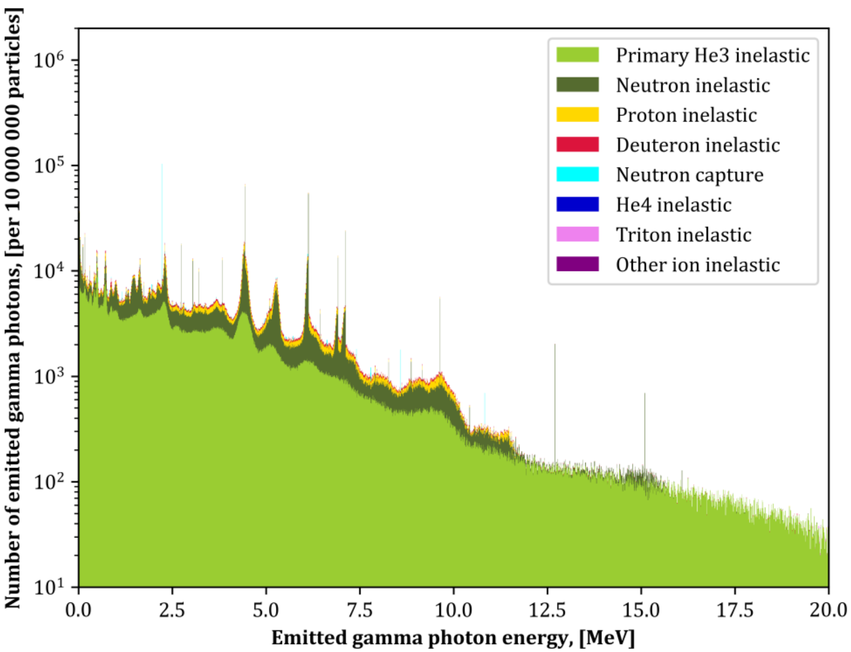


^{3}He ion beam prompt gamma emission spectrum

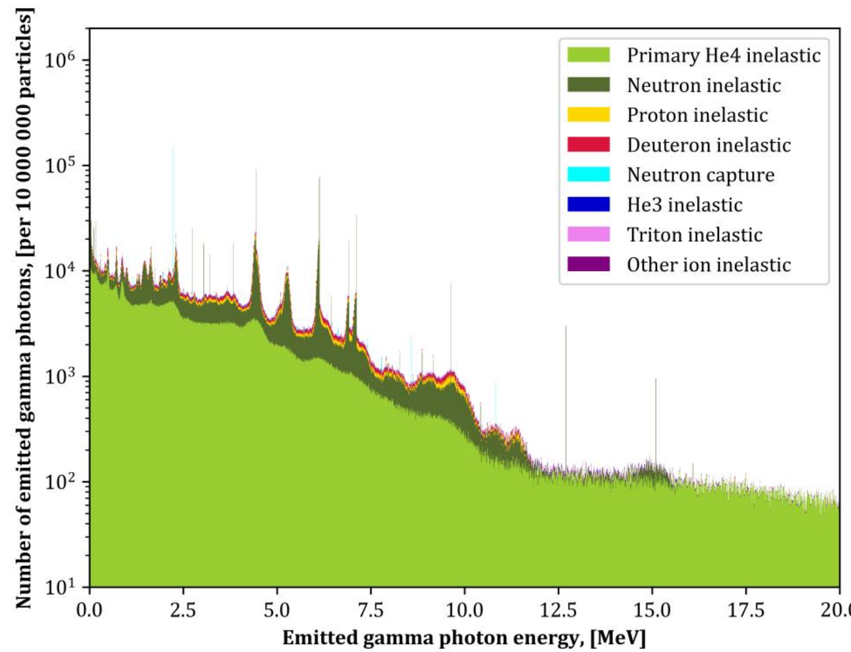


^{4}He ion beam prompt gamma emission spectrum

Results
Spectrum components

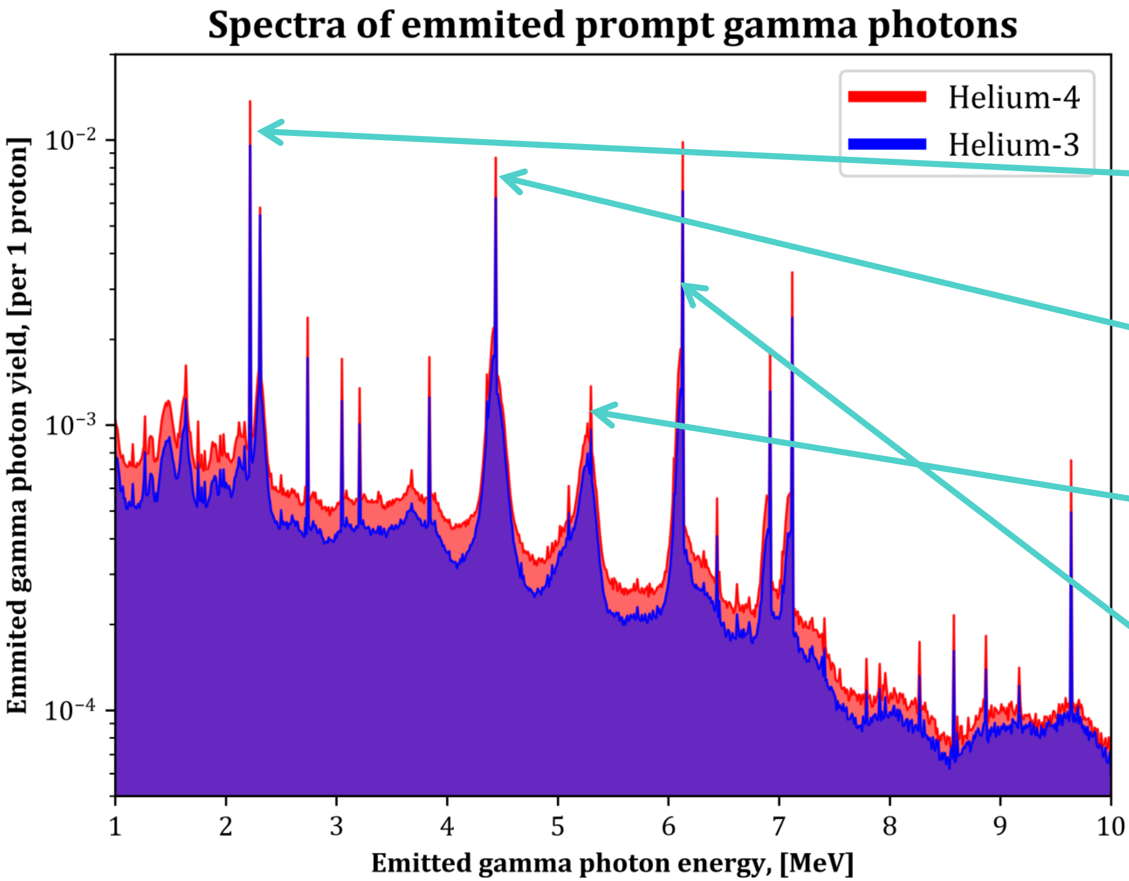


^{3}He ion beam prompt gamma emission spectrum



^{4}He ion beam prompt gamma emission spectrum

Results
Emission depth distributions



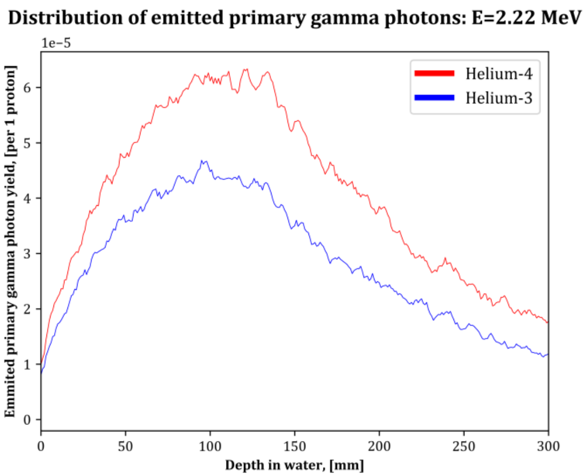
2.22 MeV: Neutron capture by hydrogen

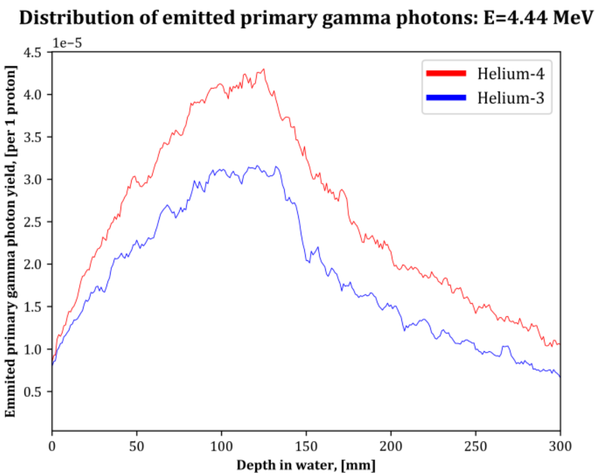
4.44 MeV: De-excitation of ^{12}C

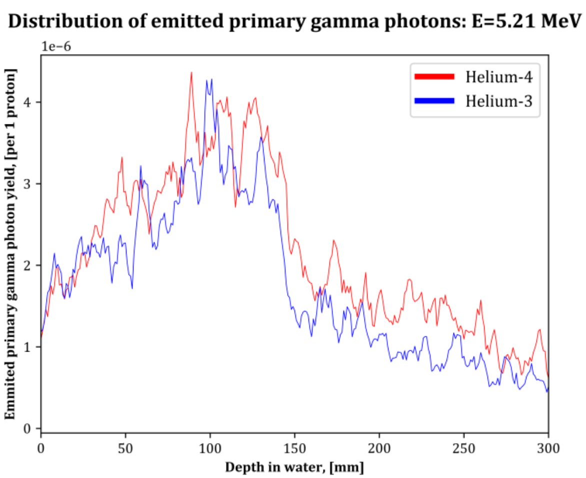
5.21 MeV: De-excitation of ^{15}O

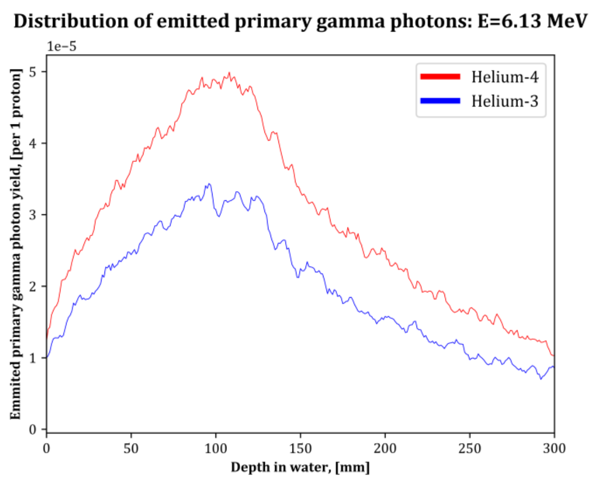
6.13 MeV: De-excitation of ^{16}O

Results
Emission depth distributions









Based on PG emission depth distributions, PG detection at **4.44** or **6.13 MeV** would be favourable due to higher signal and sharper fall-off

RĪGAS TEHNISKĀ UNIVERSITĀTE

Conclusions

- ^{4}He ion beams exhibit more favourable clinical characteristics in terms of RBE and lateral dose distribution due to scattering
- ^{3}He ion beams provide favourable physical dose distributions with decreased entrance dose, though this becomes neglible if biological optimization of dose distribution is performed
- In terms of applicability for range verification, ^{3}He ion beams provide higher signal level for PET methodology, while ^{4}He ion beams – for prompt gamma detection. Though experimental validation of this aspect would be required.

Conclusions

From accelerator physics point-of-view, the gain of creating smaller sized, more compact synchrotron ring for ^3He ion beams could be justified with the medical physics findings of this study.

1862

RĪGAS TEHNISKĀ UNIVERSITĀTE

Thank you for your attention!