New applications of positron-emitting nuclei in medical imaging and treatment at GSI

Sivaji Purushothaman
for Super-FRS Experiment Collaboration and BARB collaboration

NUSTAR Annual Meeting 2024

RIB for hadron therapy

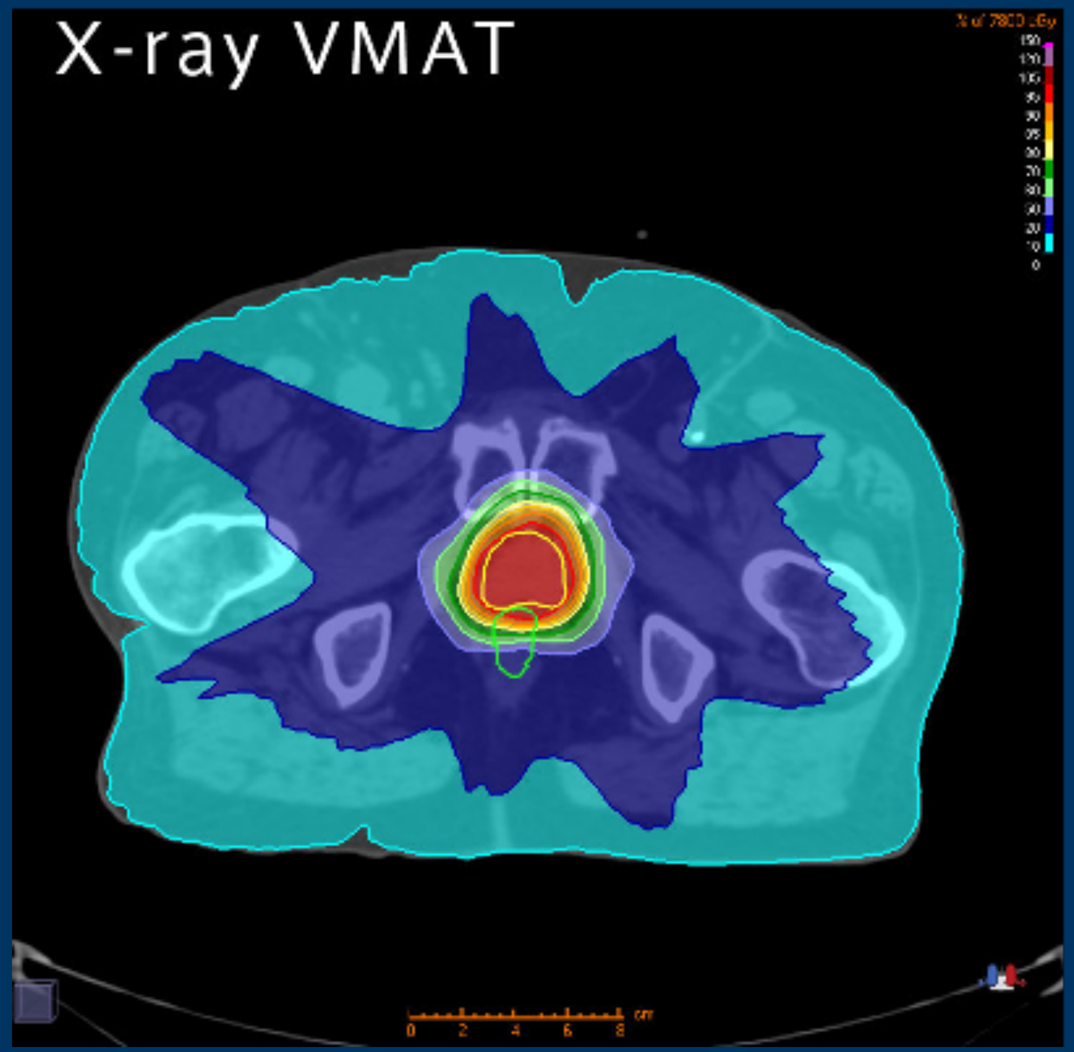
Range verification with RIB of positron emitters and PET

- **1980 – 1992** — **LBNL, US**
  Positron emitting RIB
  As low dose probe beam
- **1990 – 1992** — **GSI, Germany**
  Initial investigations on PET imaging using positron emitting RIB at FRS
- **2000** — **HIMAC, Japan**
  Investigations on
  Positron emitting isotopes of C & O
- **2015** — **CERN-ISOLDE ,KU Leuven, Belgium & Med Austron, Austria**
  mass separated 11Carbon for PET-aided hadron **therapy**
- **2021** — **GSI, Germany**
  Biomedical Applications of Radioactive ion Beams
  ERC Advanced Grant BARB

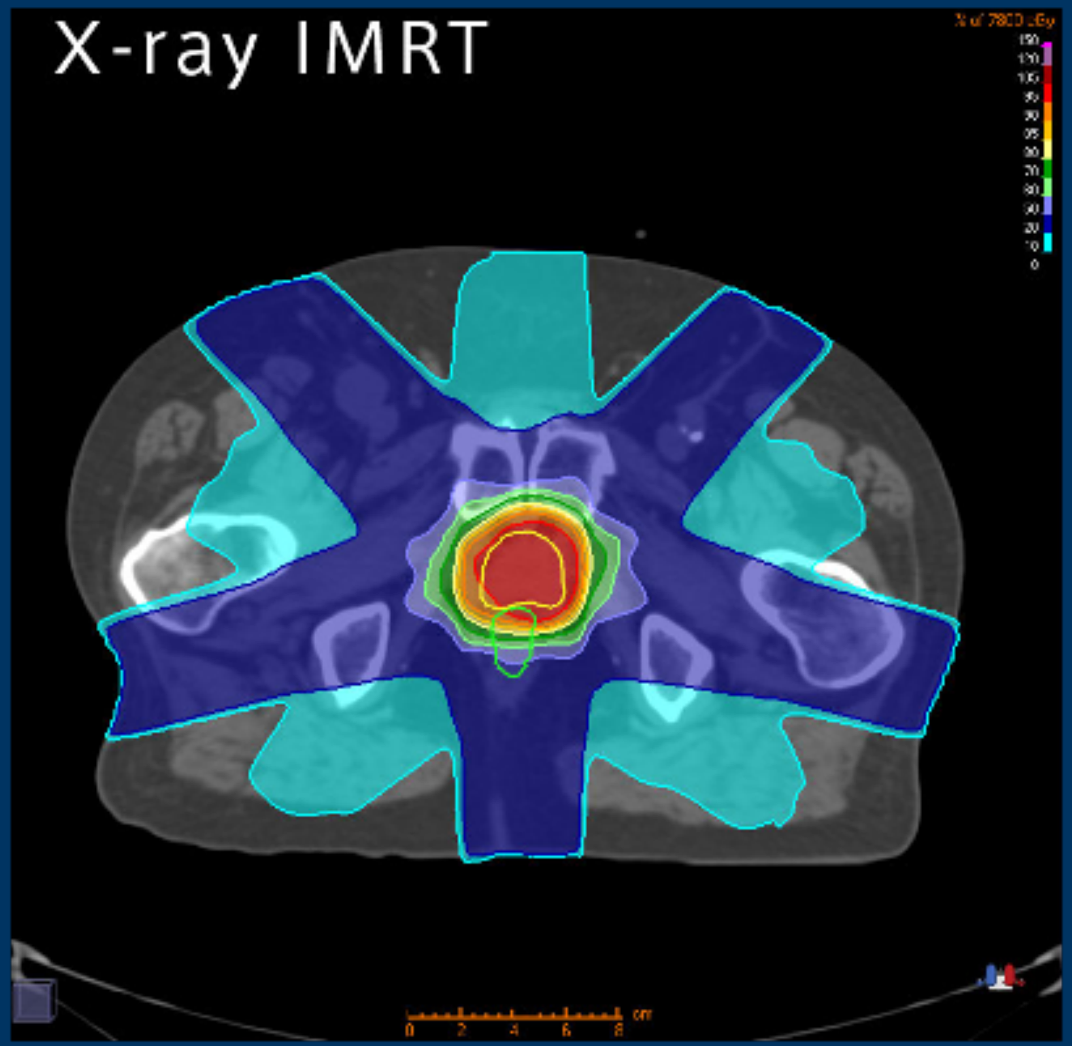
Ion beam therapy : Benefits

Photon Therapy

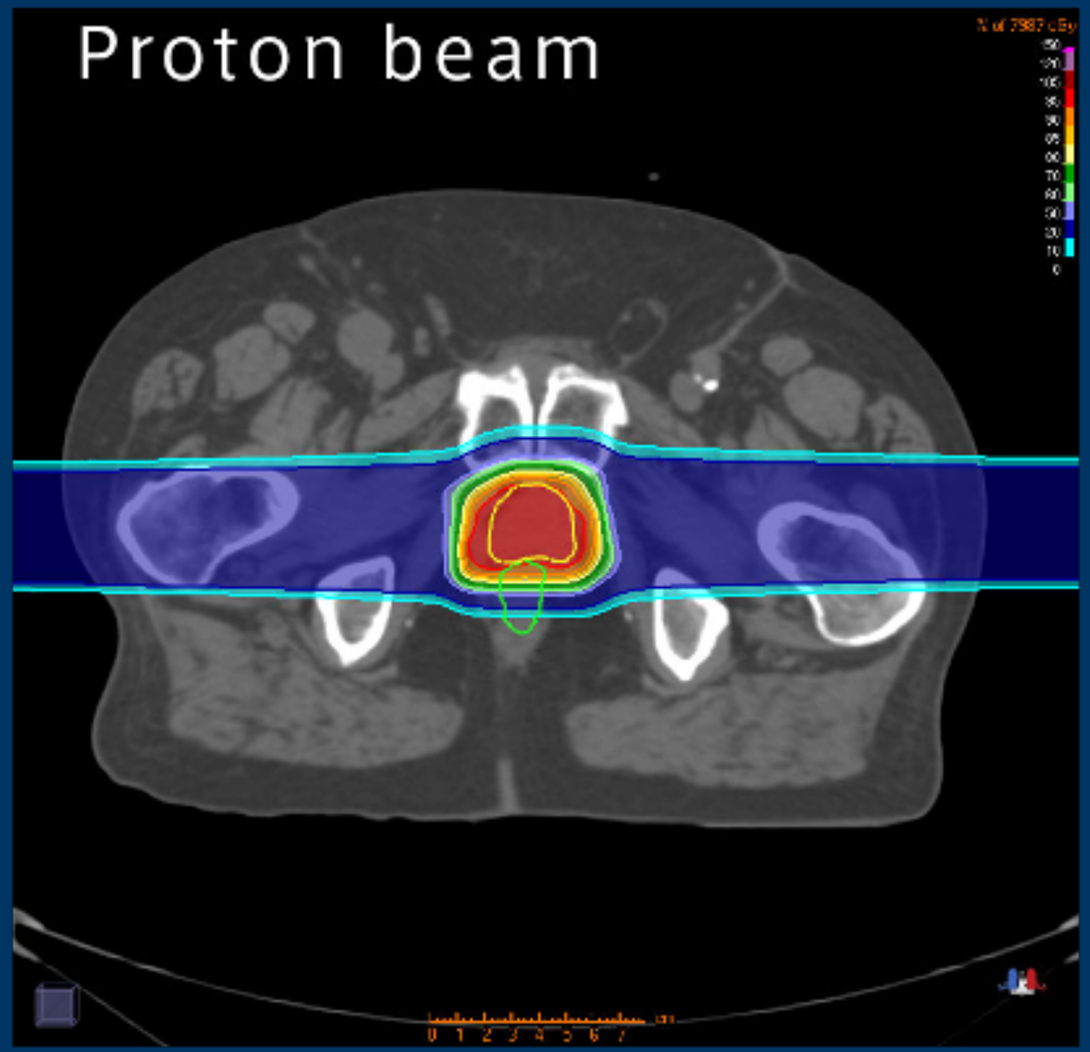
Volumetric Modulated Arc Therapy

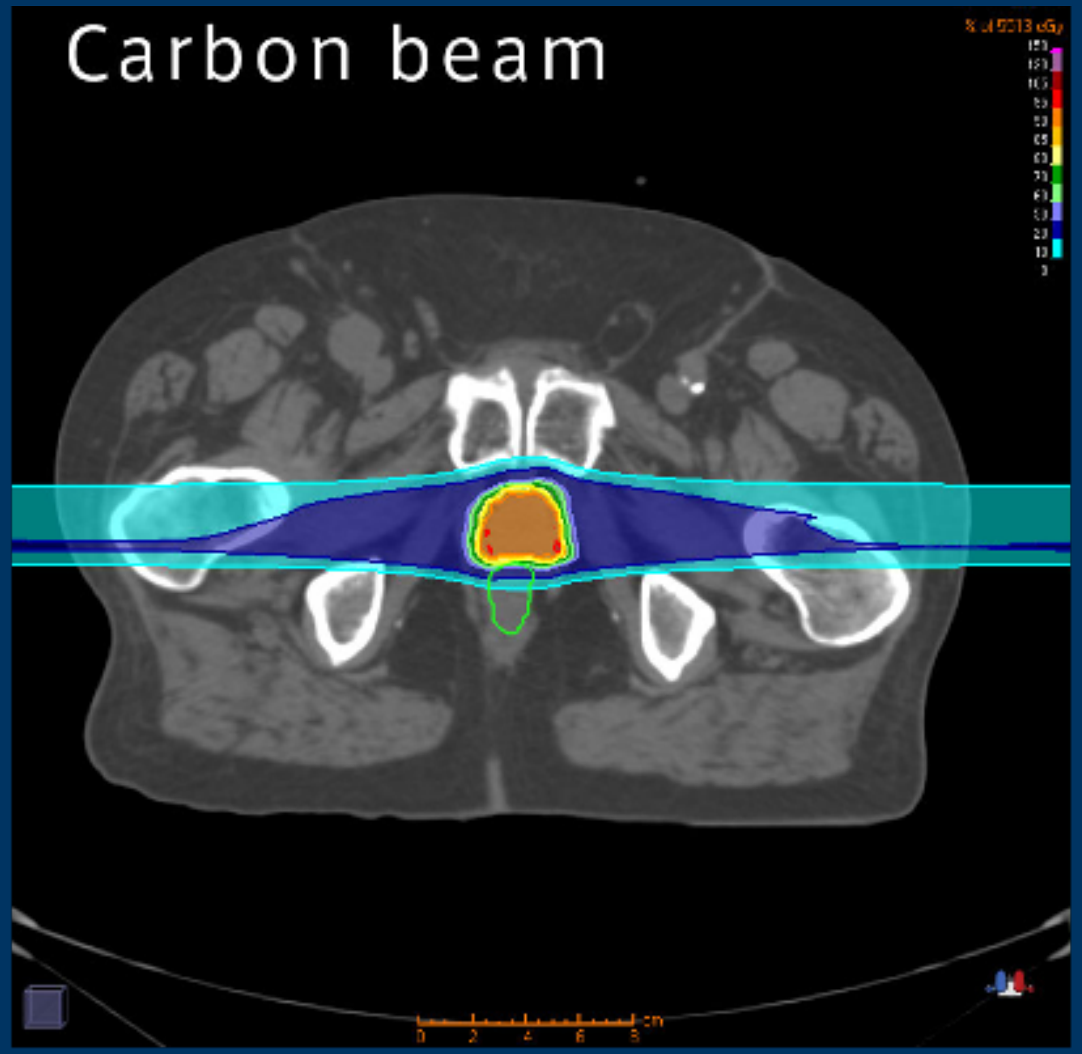


Intensity-modulated radiotherapy



Hadron Therapy





- High tumour dose, normal tissue sparing
- Effective for radio-resistant tumours
- Effective against hypoxic tumour cells

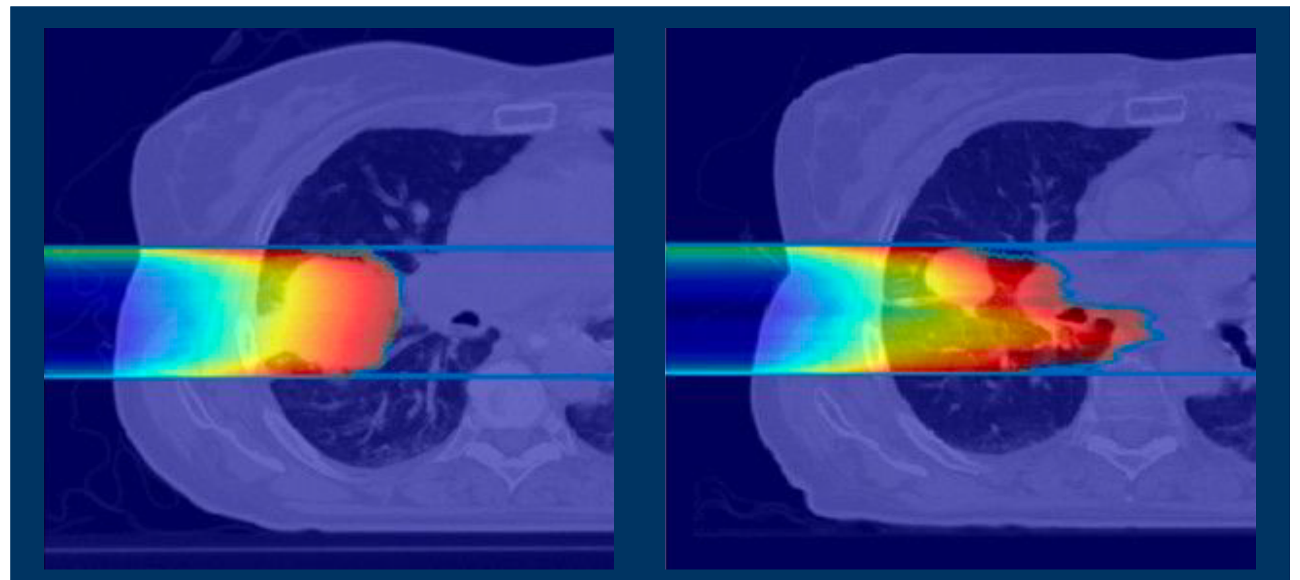
Image courtesy: Osaka Heavy Ion Therapy Center & Durante & Loeffler, Nature Rev Clin Oncol 2010

Ion beam therapy : Challenges

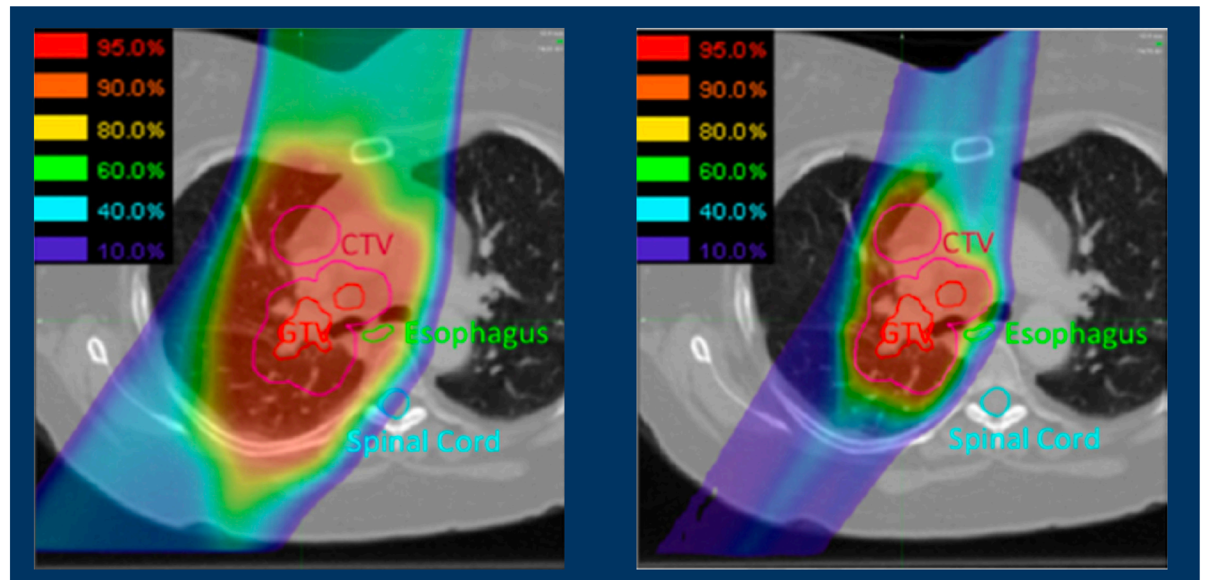
Range uncertainties

Highly conformal ▶Low tolerance for treatment planning error

- Inherent uncertainties in the conversion from X-ray CT data to particle range
- Anatomical changes
- Quality of the CT
- Daily errors: patient setup and alignment,…



Planning CT CT after 5 weeks



With 1 cm margin No margin

Typical uncertainties assumed in robust treatment planning for 12C ion therapy

Setup uncertainty of ±3 mm ±2% of range

Tony Lomax, Oxford 2008

Durante & Flanz, Semin. Oncol. 2019

Range uncertainties: Way forward

Tumour tracking & Treatment verification

Tumour tracking
4DCT
Beam tracking
…

Radiotherapy with positron emitters

Range verification with RIB of positron emitters and PET

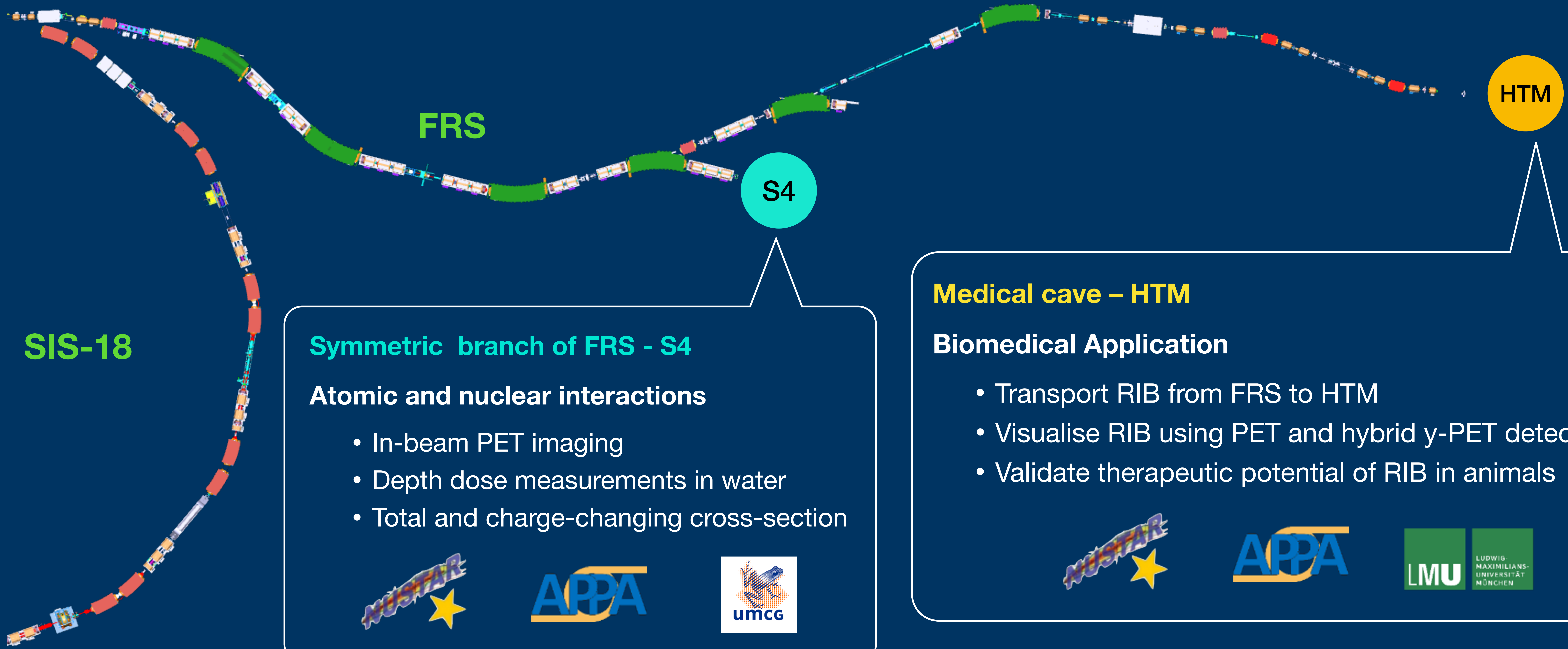
- Off-line PET dosimetry
- In-beam PET dosimetry
- Prompt radiation measurement

Biomedical Applications of Radioactive ion Beams
ERC Advanced Grant
PI: Prof Marco Durante, Co-PI: Prof. Katia Parodi

Riboldi et al., Lancet Oncol. 2012

BARB experiments with RIB

Positron emitting beams



Symmetric branch of FRS - S4

Atomic and nuclear interactions

- In-beam PET imaging
- Depth dose measurements in water
- Total and charge-changing cross-section

Medical cave – HTM

Biomedical Application

- Transport RIB from FRS to HTM
- Visualise RIB using PET and hybrid y-PET detector
- Validate therapeutic potential of RIB in animals

Boscolo, Daria, et al. Front. Oncol. 11 (2021)

Quasi-real-time range Monitoring

Which is the best positron emitting therapy beam

Required qualities

Range verification

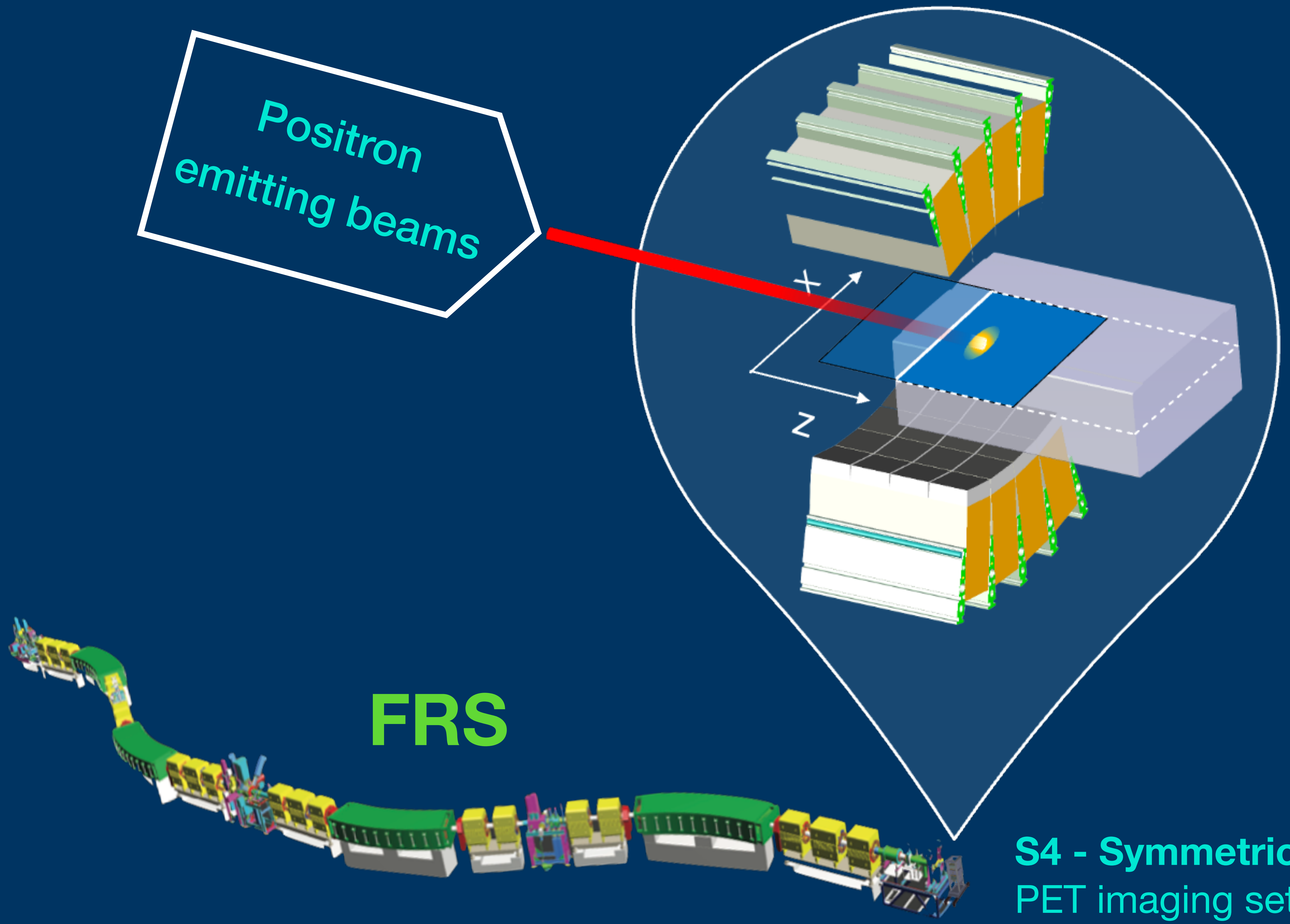
- Achieved with the lowest possible dose
- As early as possible

Availability of therapeutic-quality beam

- Intensity
- Purity

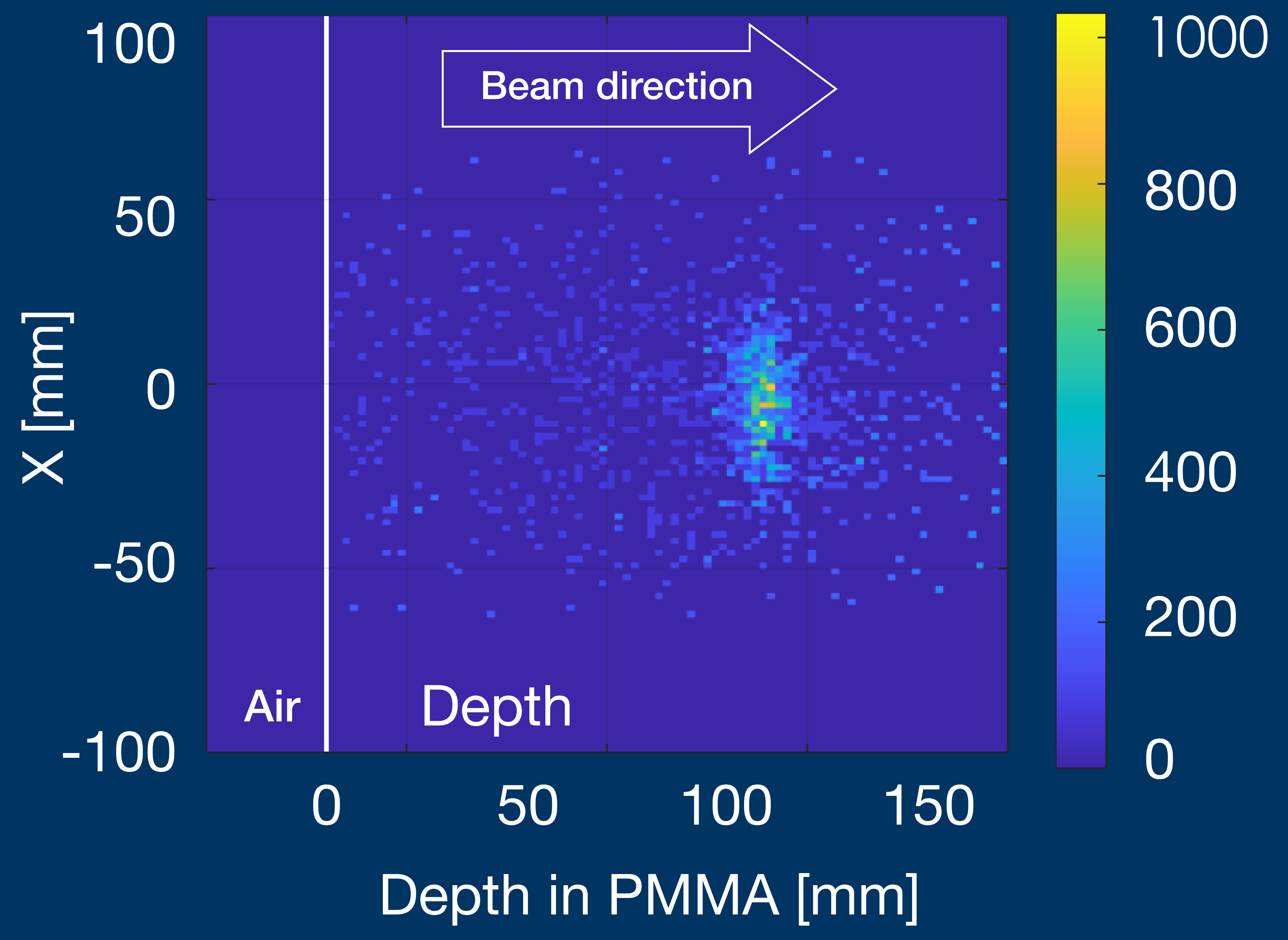
PET imaging at FRS

Quasi-real-time range Monitoring



S4 - Symmetric branch of FRS
PET imaging setup

2D PET image of 14O
After 4 implantation cycles



1/6th of a Siemens Biograph mCT clinical scanner

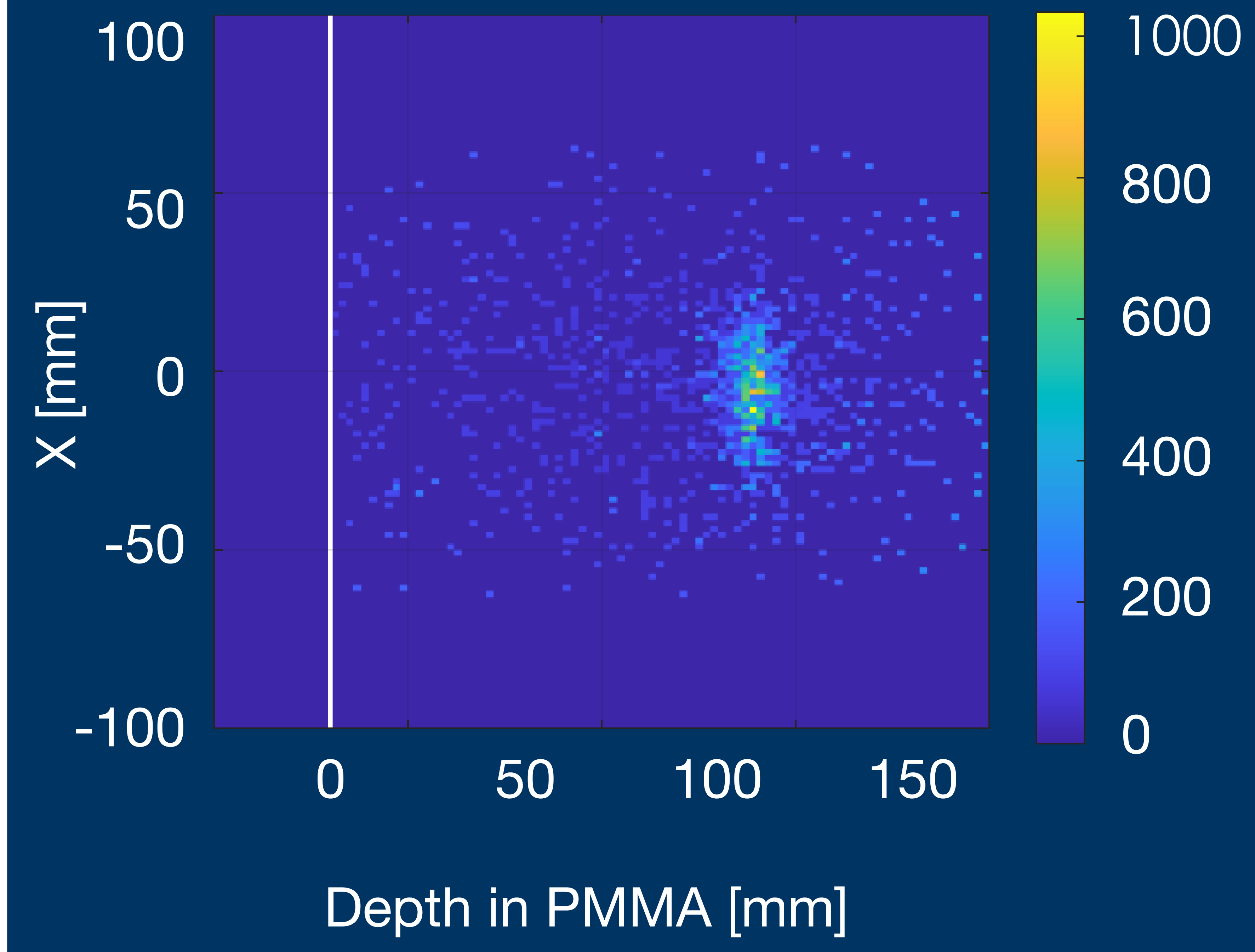
Peter Dendooven

Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023)
Kostyleva, Daria, et al. Phys. Med. Biol 1 (2023)

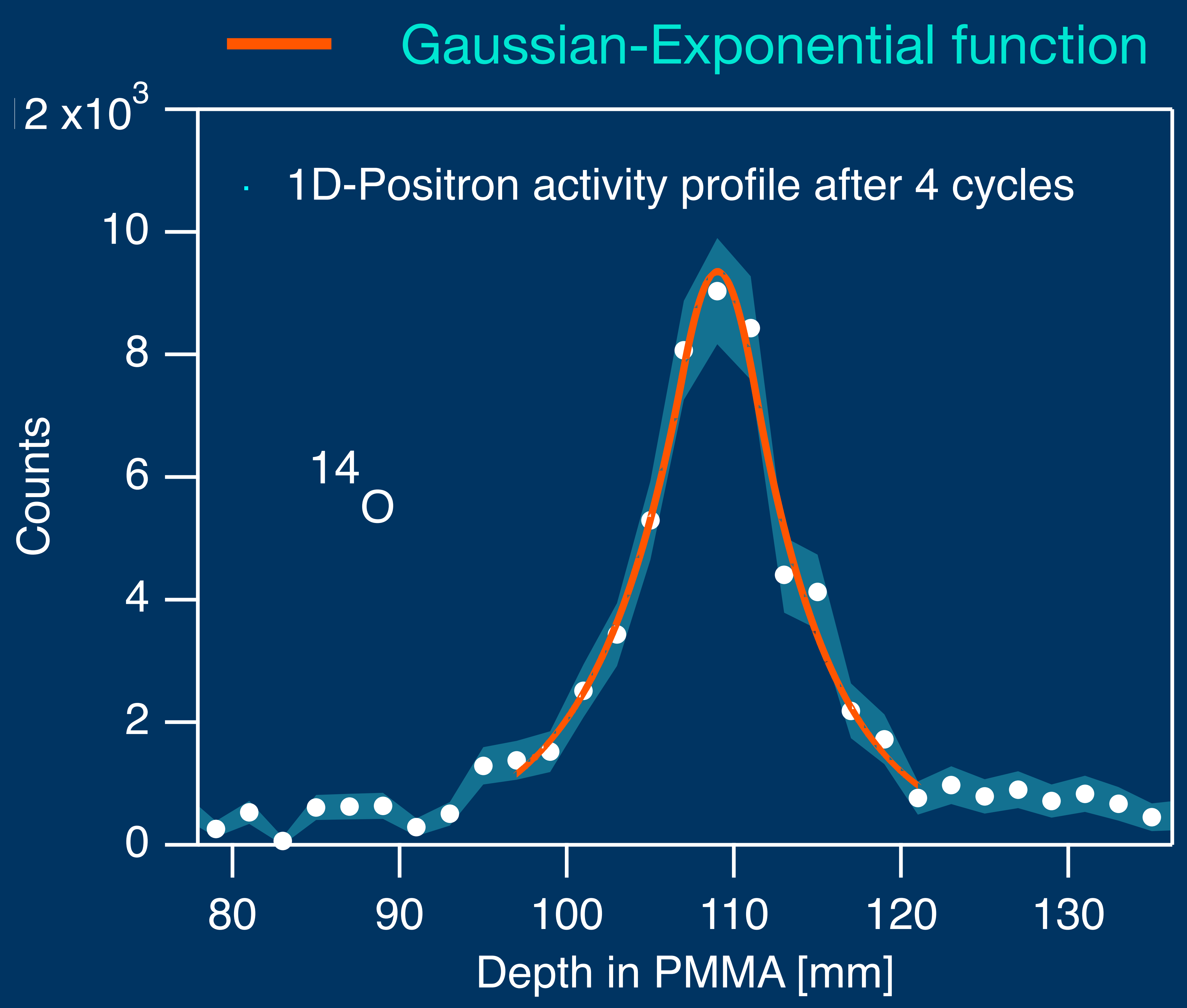
Evaluation of the positron activity

Peak position and its uncertainty

2D PET image of 14O after 4 implantation cycles

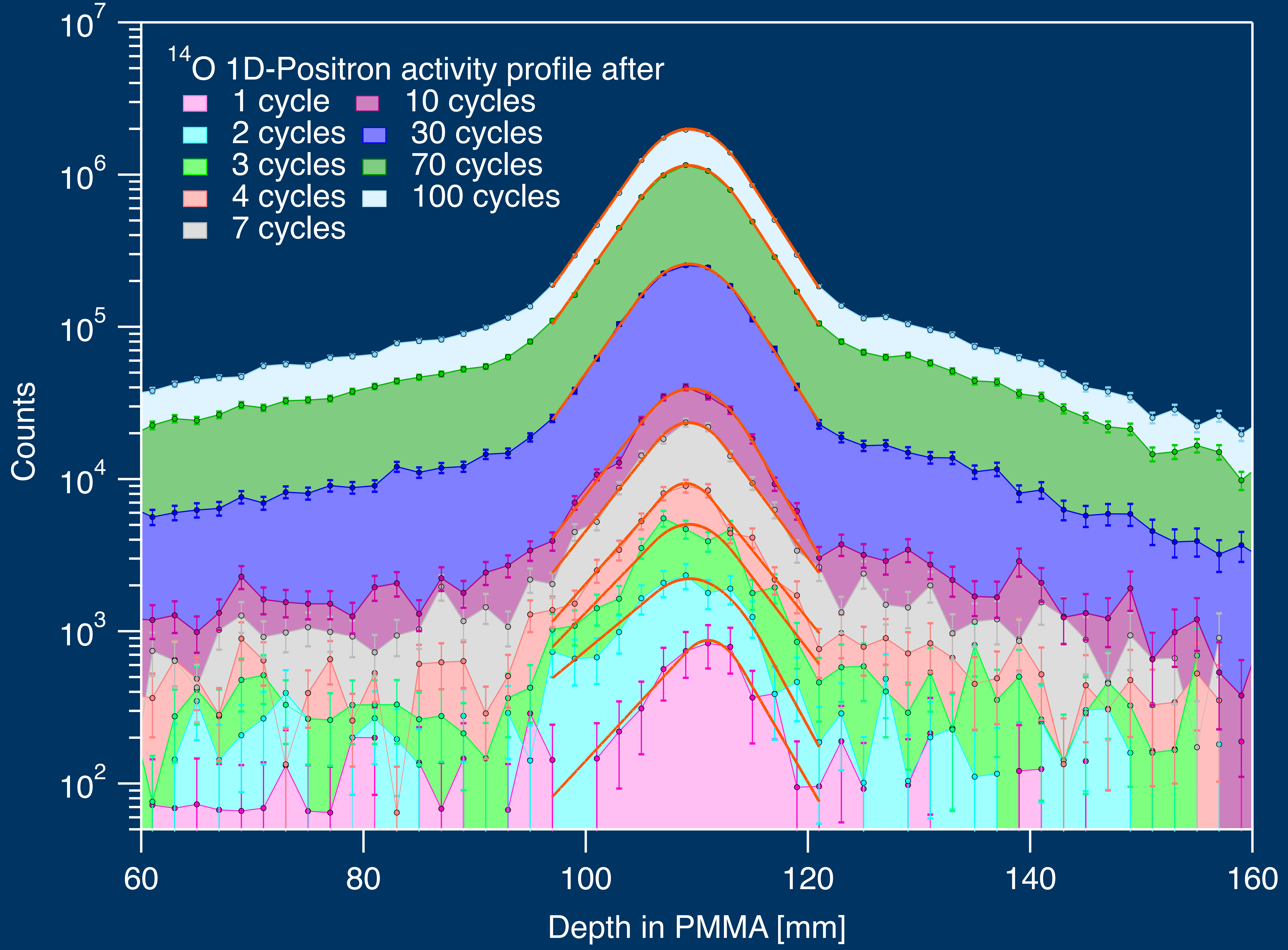


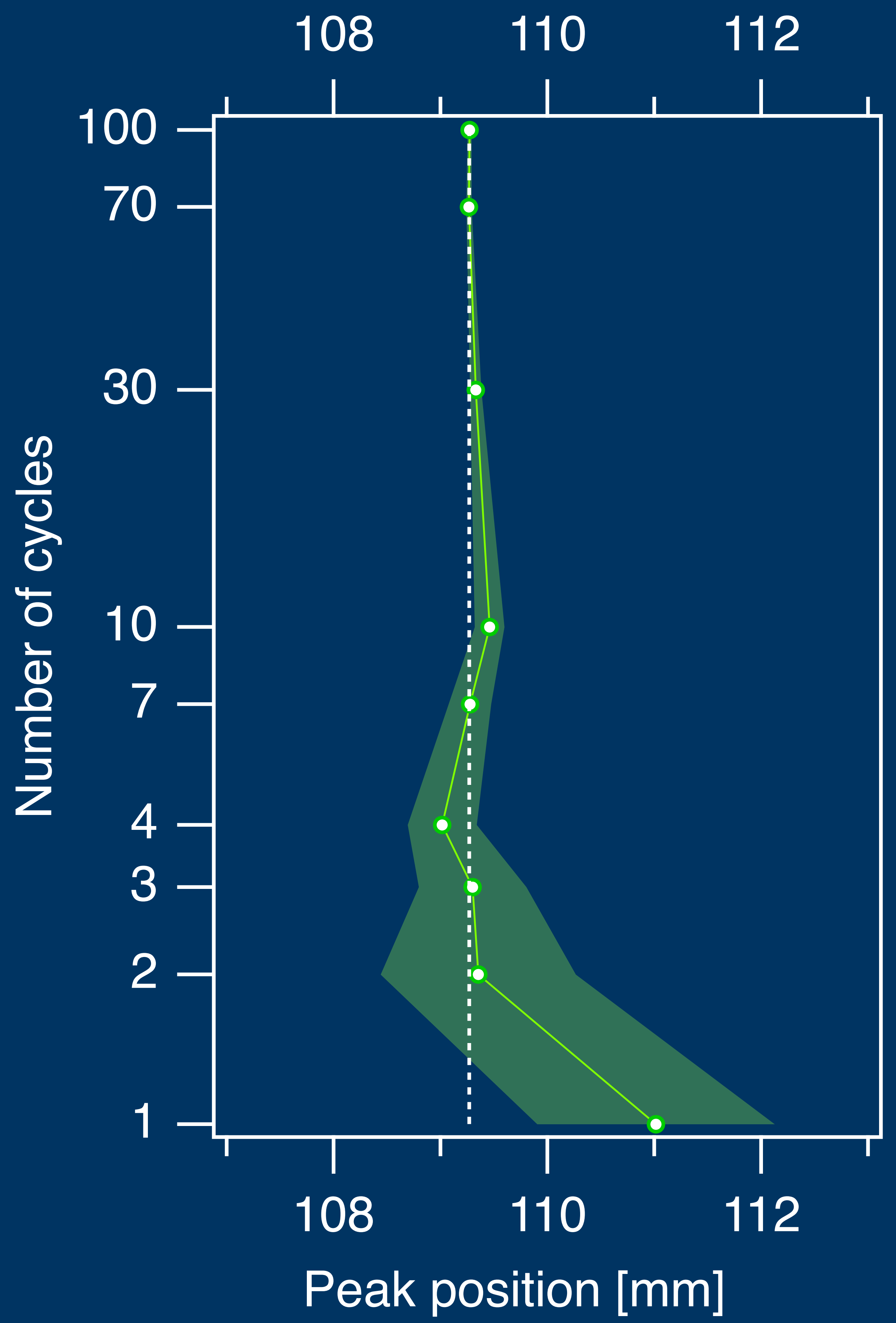
Projection to the beam axis



Evaluation of the positron activity

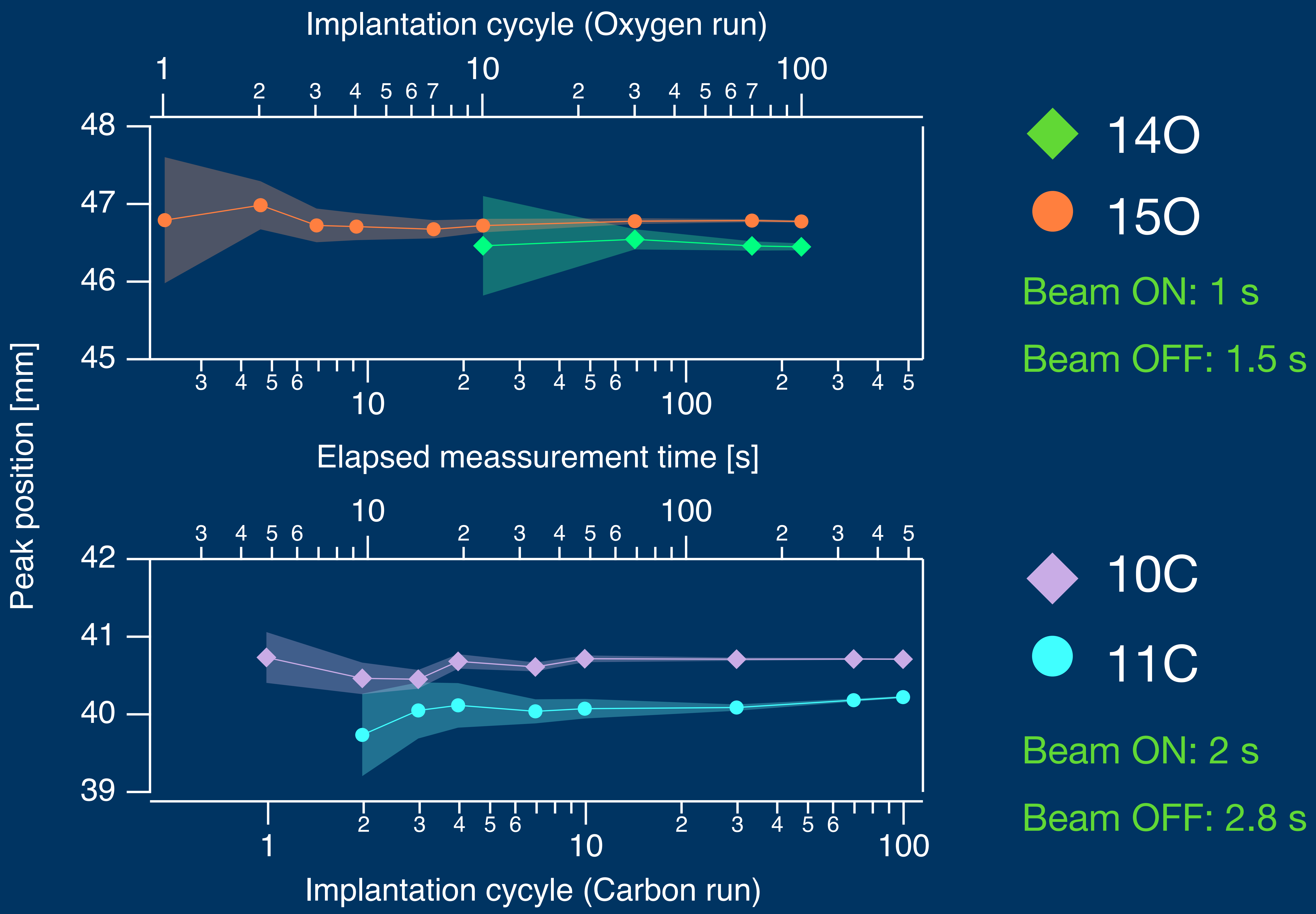
Cumulative positron activity profiles 1D activity profiles during irradiation





Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023

Evolution of positron activity peak



Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023
Kostyleva, Daria, et al. Phys. Med. Biol 1 (2023).)

Quasi-real-time range monitoring

Impact of half lives, beam time structure and intensity

Beam intensity

→ Production cross section

16O → Be

- **15O : 43 mb**
- 14O : 1.2 mb

12C → Be

- 11C : 46.7 mb
- 10C : 4.3 mb

?

What is the Best candidate for Quasi-real-time Range monitoring

Half life

11C : 1220.84 s

15O : 122.24 s

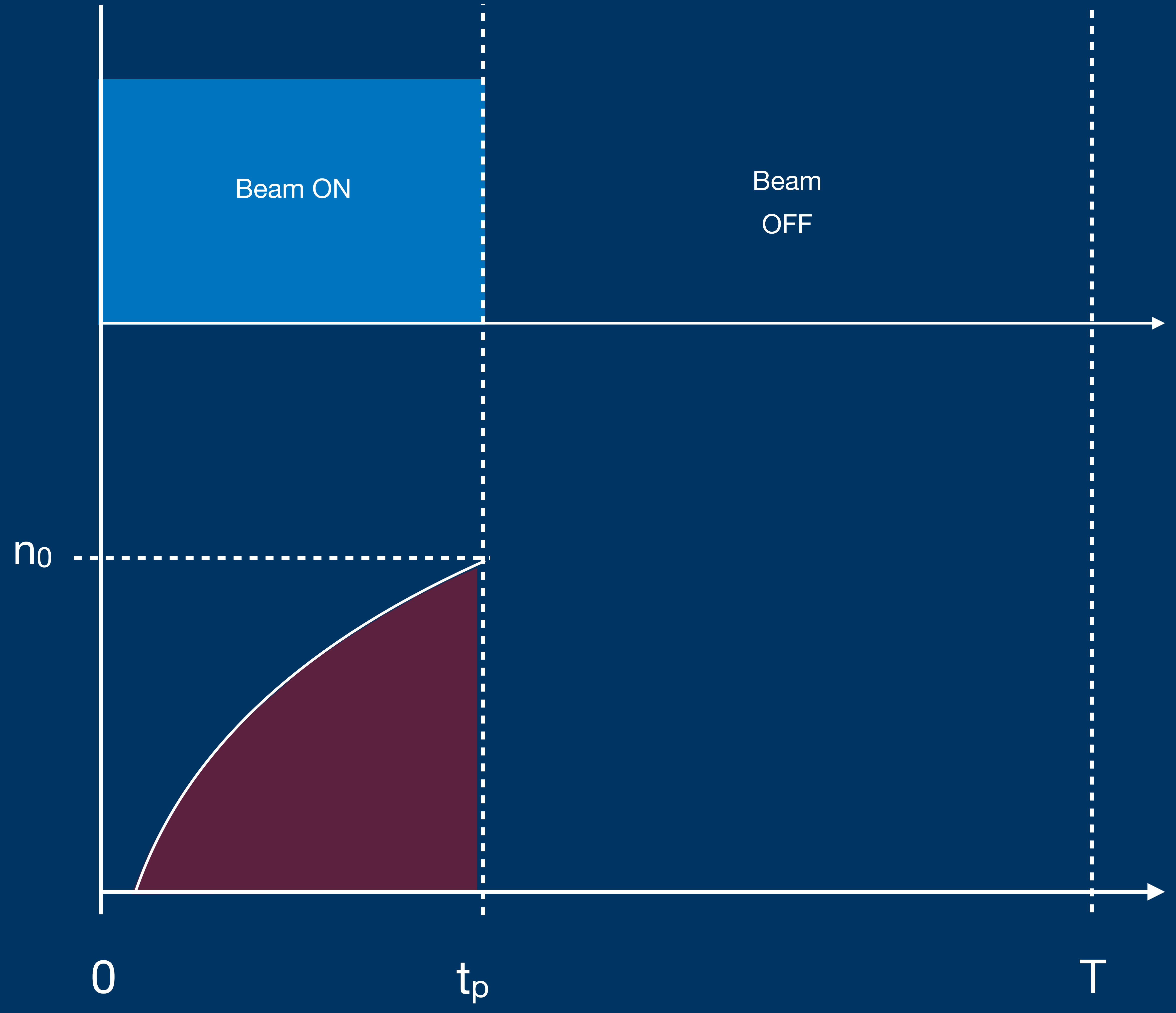
14O : 70.606 s

10C : 19.31 s

Beam pulse time structure

Quasi-real-time range monitoring

Impact of half lives, beam time structure and intensity



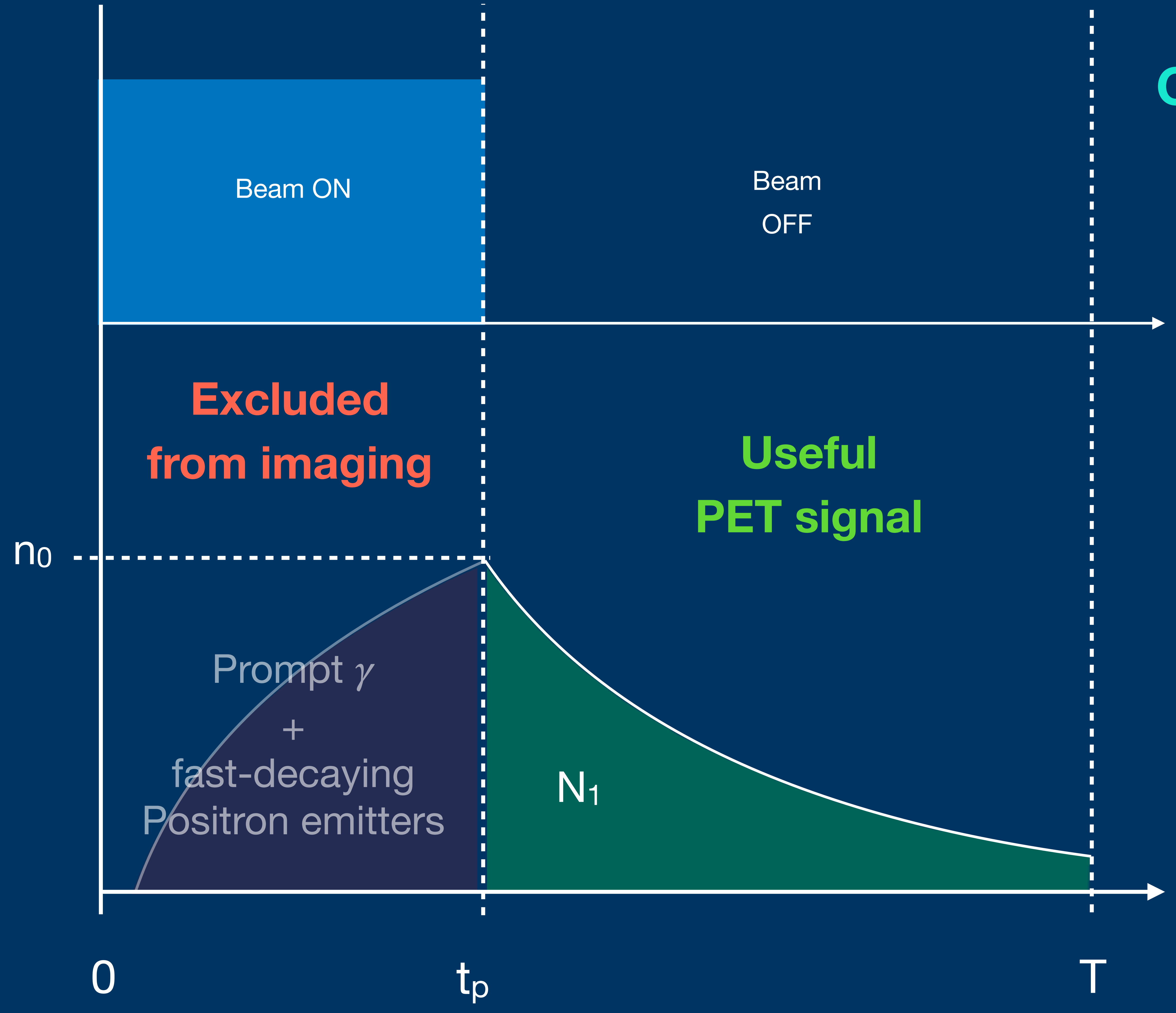
The amount of positron emitters left at the end of the pulse

$$n_0 \propto \frac{\sigma}{\lambda t_p}\left[1 - e^{-\lambda t_p}\right]$$

Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023)

Quasi-real-time range monitoring

Impact of half lives, beam time structure and intensity



Coincidence event yield during the beam pause

After *1* implantation cycle

$$N_1 \propto n_0 \left[1 - e^{-\lambda(T-t_p)}\right]$$

After *n* implantation cycles

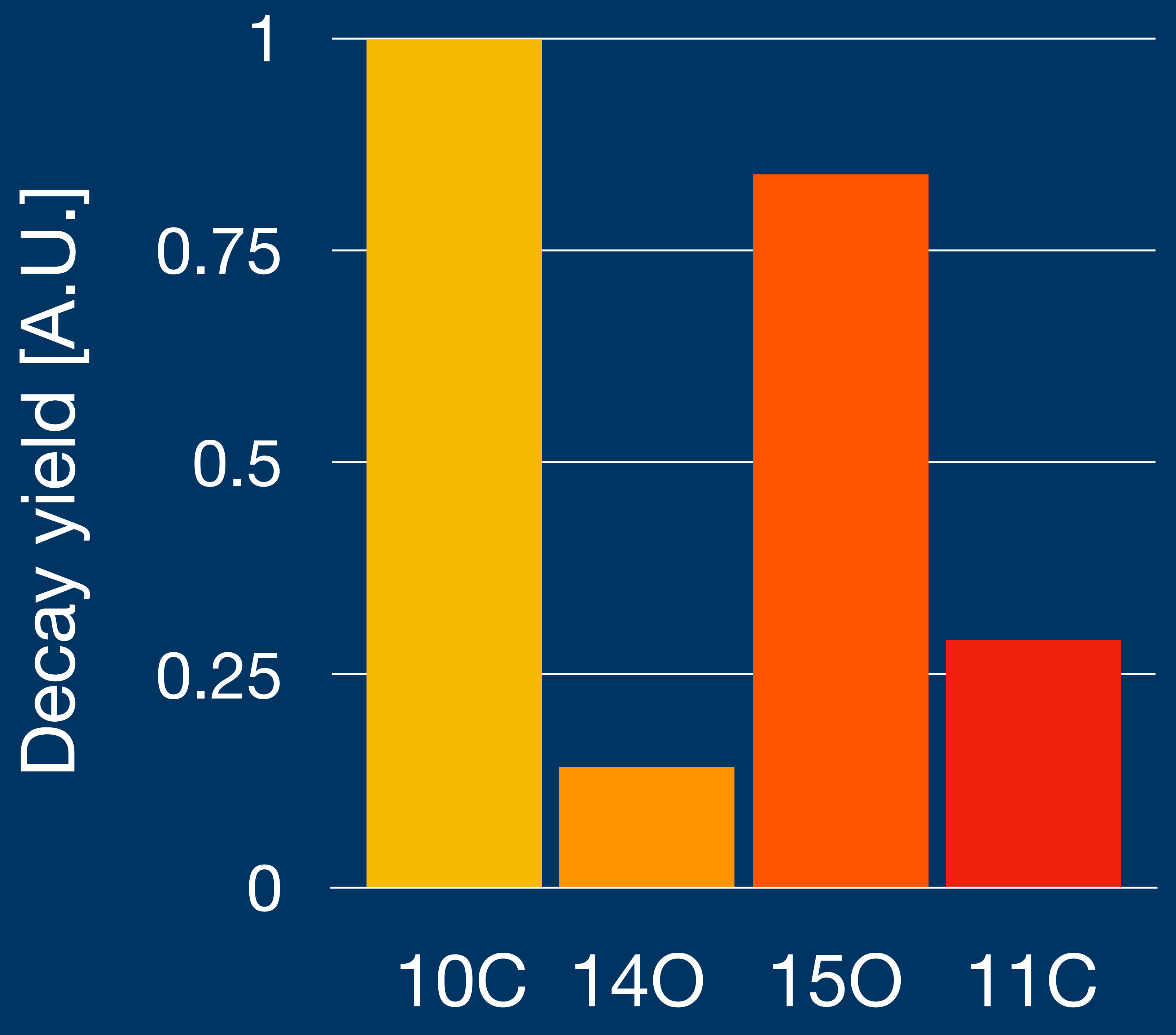
$$N_n \propto N_1 \sum_{j=0}^{(n-1)} (n-j)e^{-\lambda jT}$$

Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023)

Quasi-real-time range monitoring

Comparison of therapy relevant positron emitters of oxygen and carbon

Time structure from experiment (n=1)



14O & 15O

Beam ON: 1 s

Beam OFF: 1.5 s

10C & 11C

Beam ON: 2 s

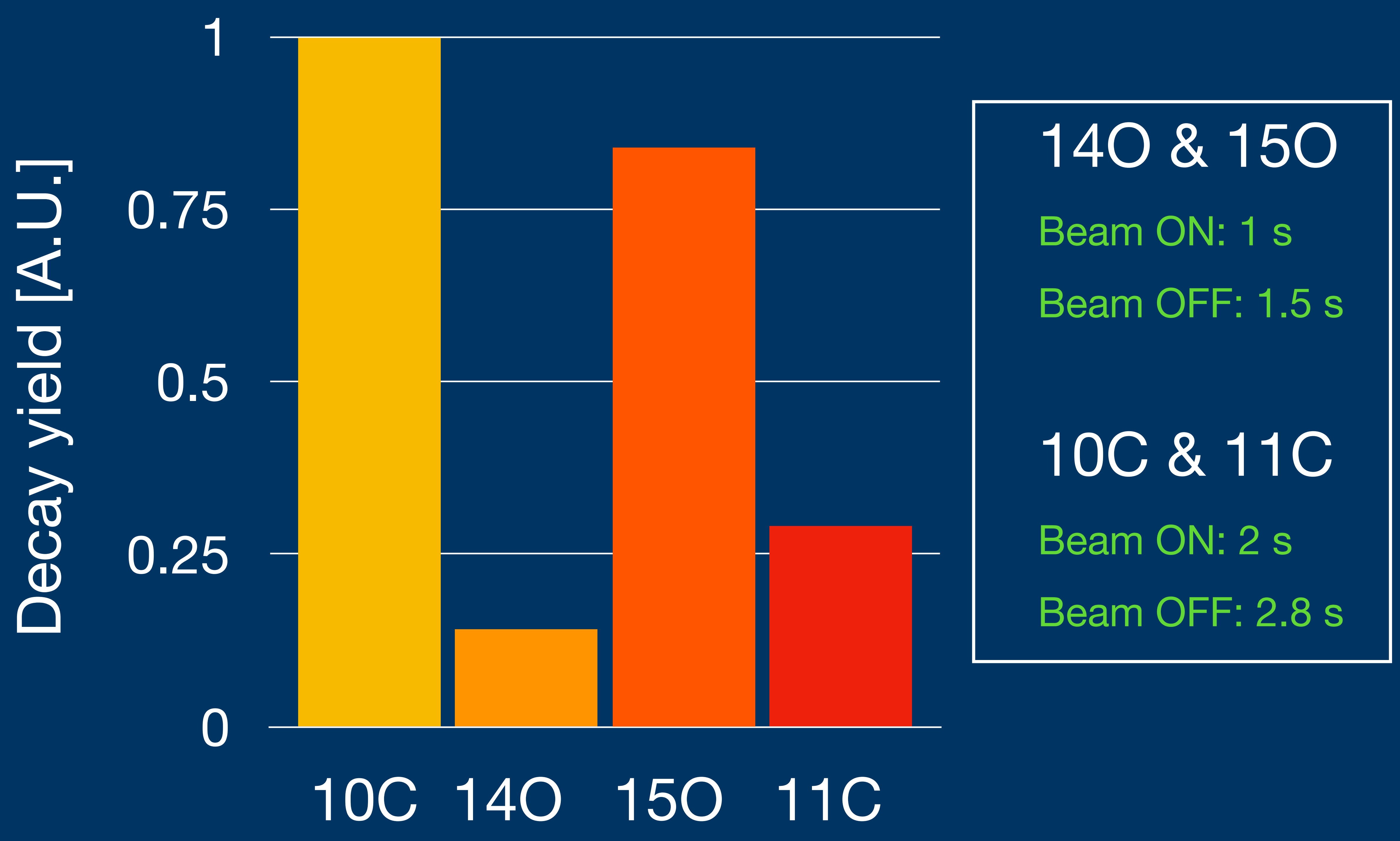
Beam OFF: 2.8 s

Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023)

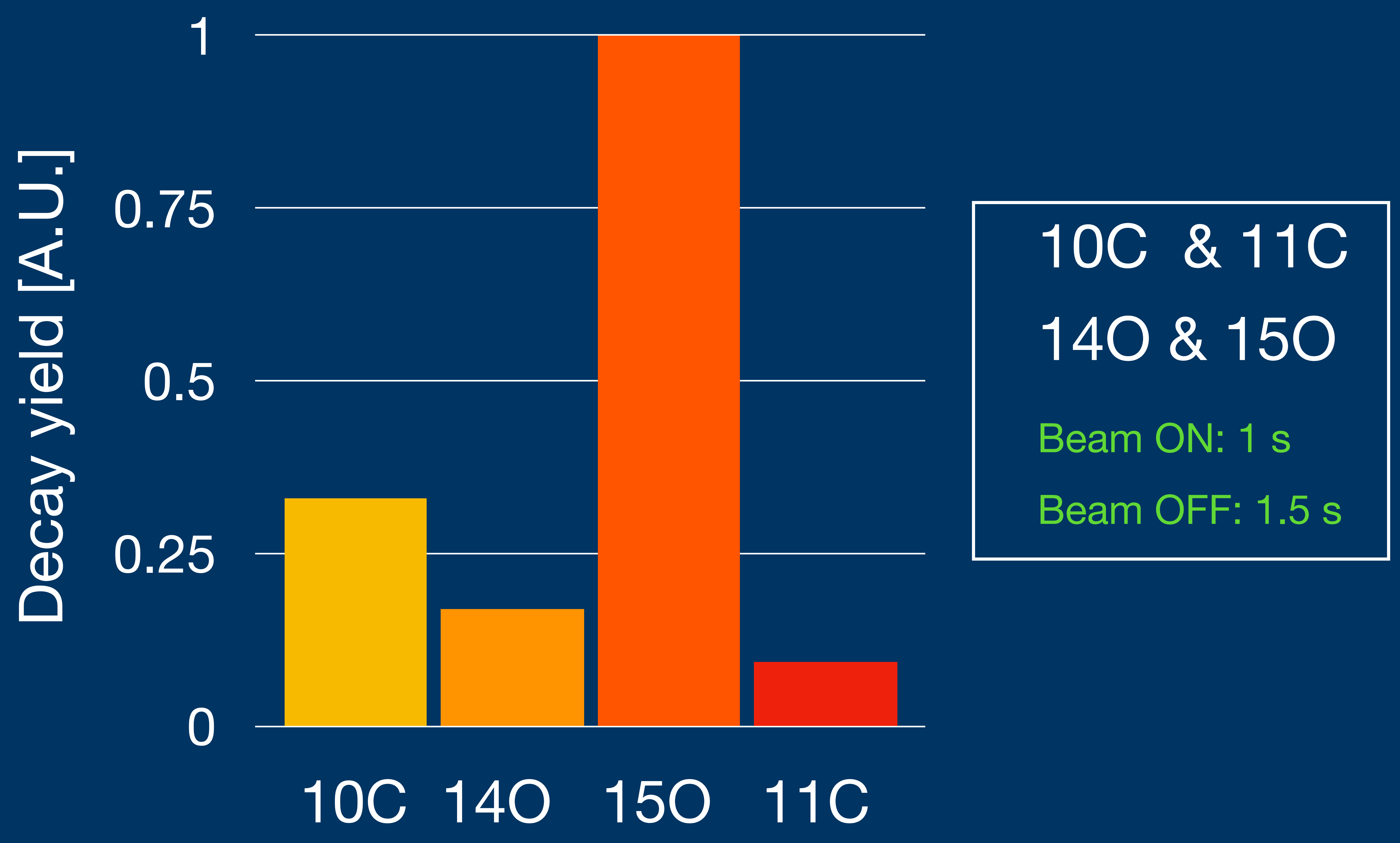
Quasi-real-time range monitoring

Comparison of therapy relevant positron emitters of oxygen and carbon

Time structure from experiment (n=1)



If beam time structure was same (n=1)



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Quasi-real-time range monitoring

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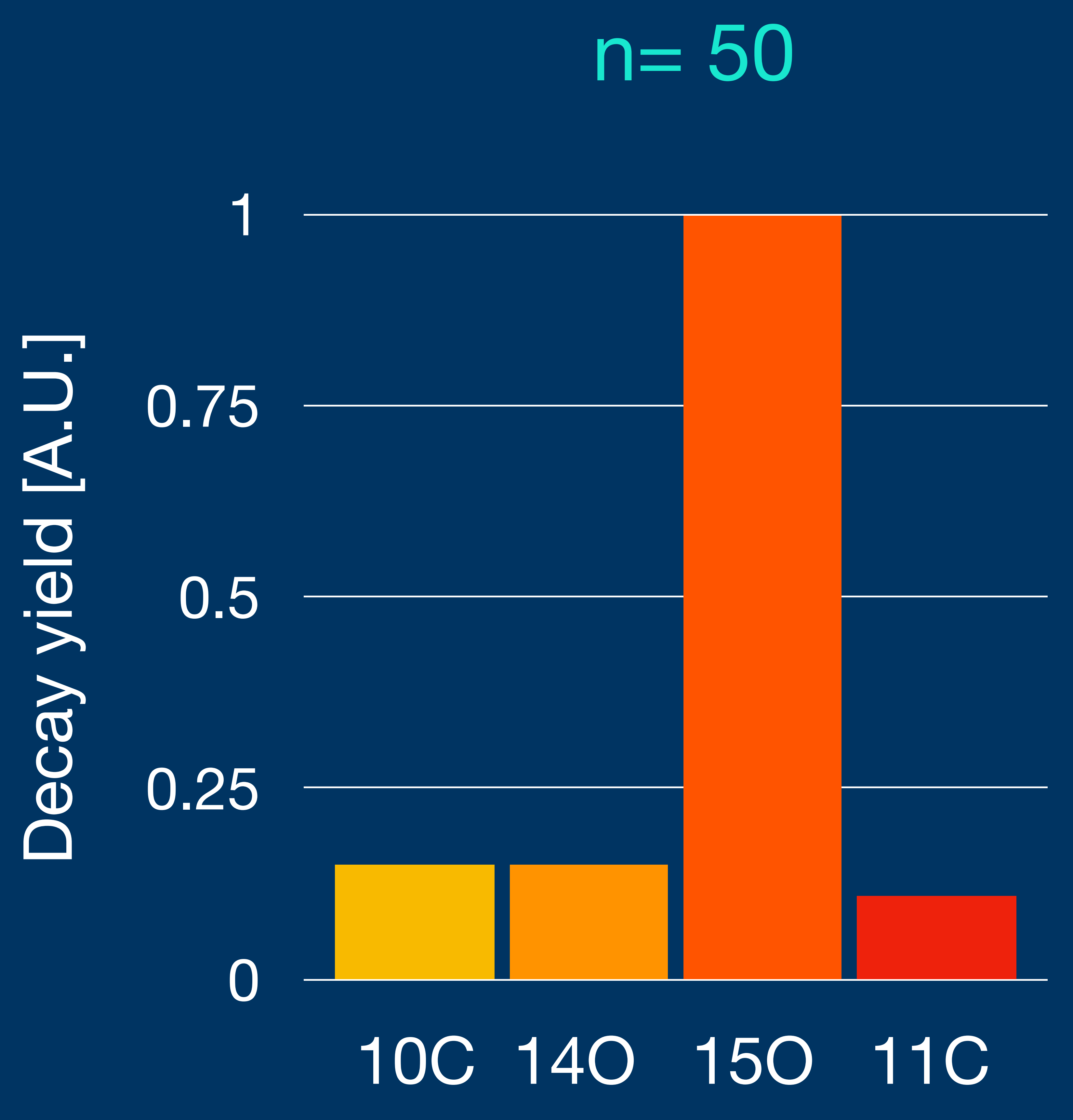
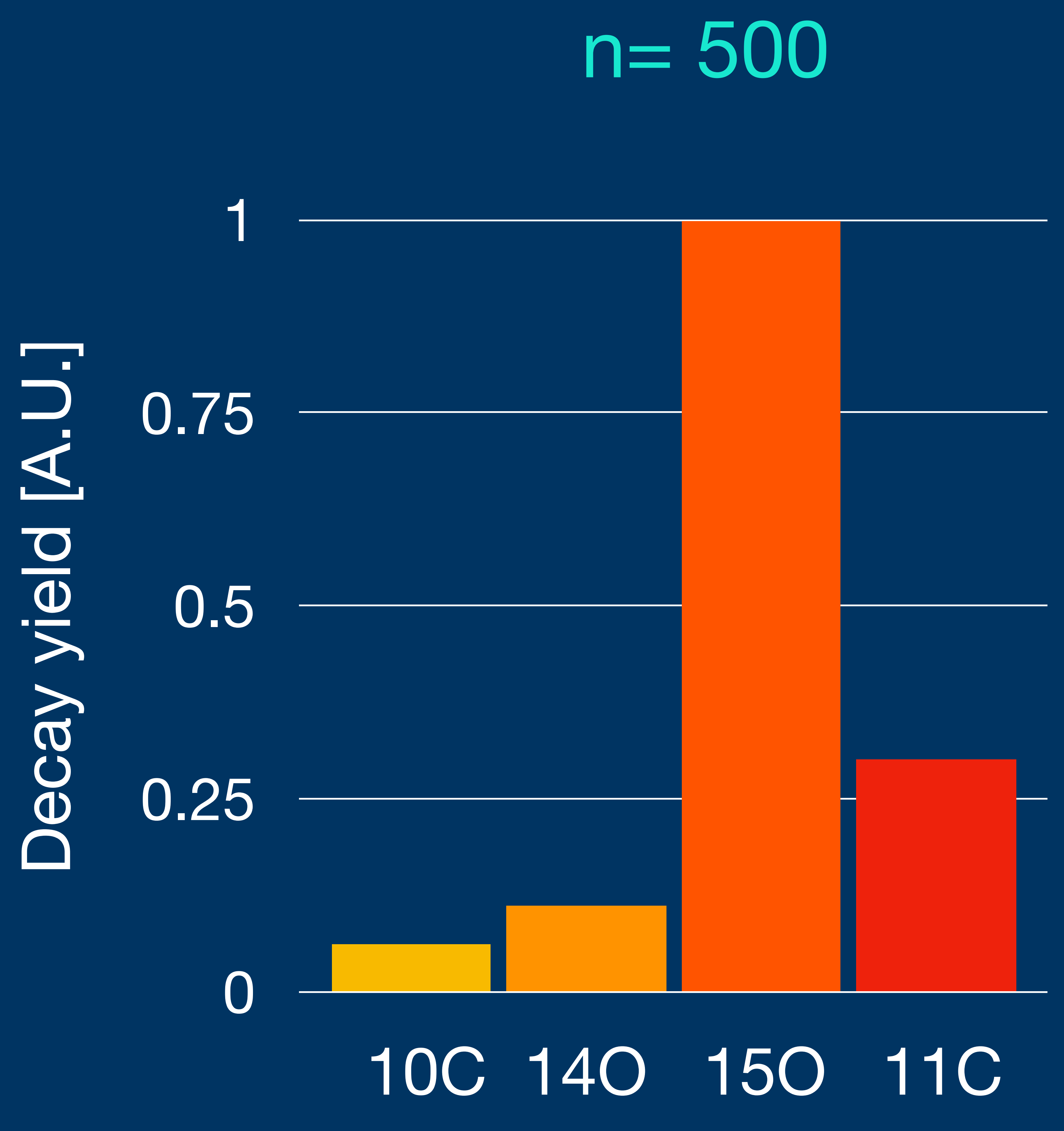


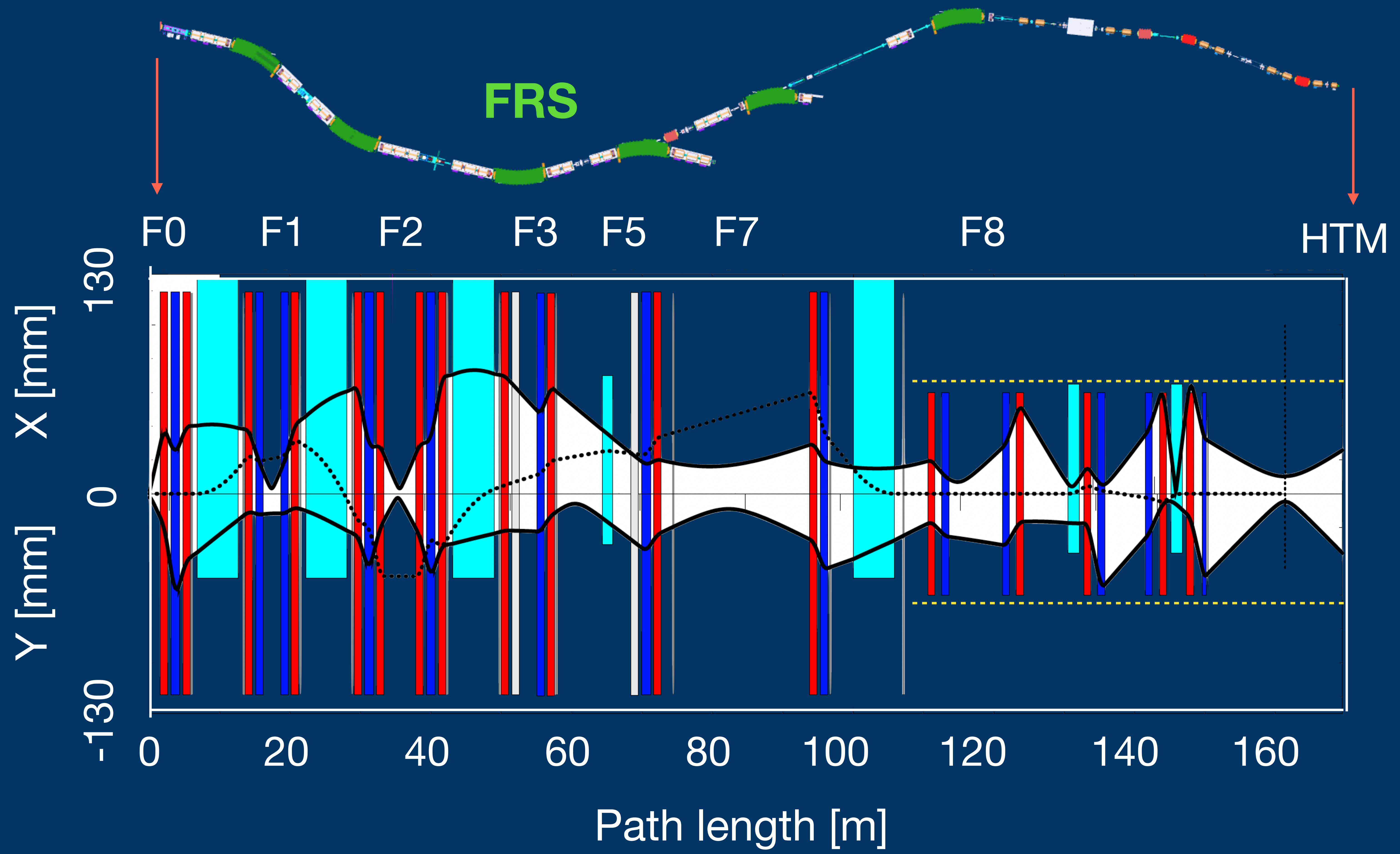
10C & 11C
14O & 15O
Beam ON: 1 s
Beam OFF: 1.5 s



Purushothaman, Sivaji, et al., Sci Rep 13, 18788 (2023)

BARB Biomedical experiments

RIB transport from FRS to Medical cave (HTM)



Challenging!

Reduced aperture from F8

200 mm ➞ 120 mm

Successful transport of

15O and 11C to HTM

Measured conversion efficiency

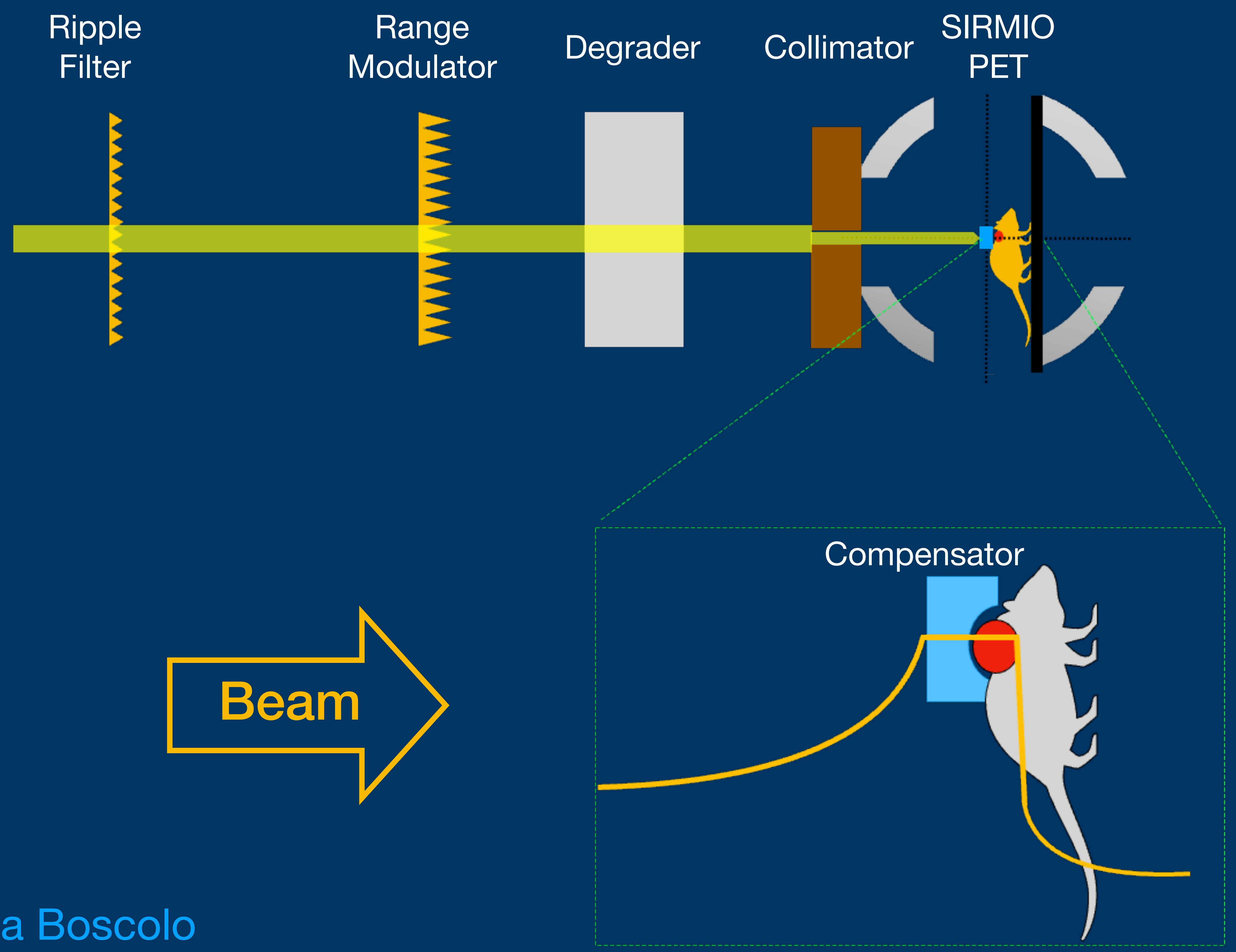
~ 3 $\times 10^{-4}$ 15O ions/16O ion in SIS 18

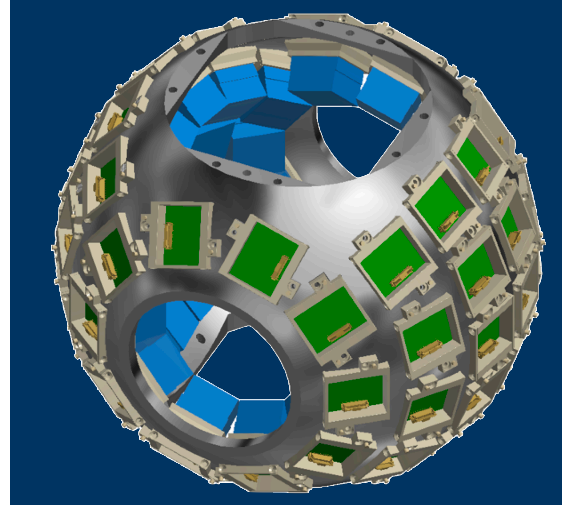
Hans Geissel
Bernhard Franczak

Emma Haettner, et al. NIM-B 541 (2023)

BARB Biomedical experiments

RIBs for therapy: Can we shrink the margin with the RIBs?

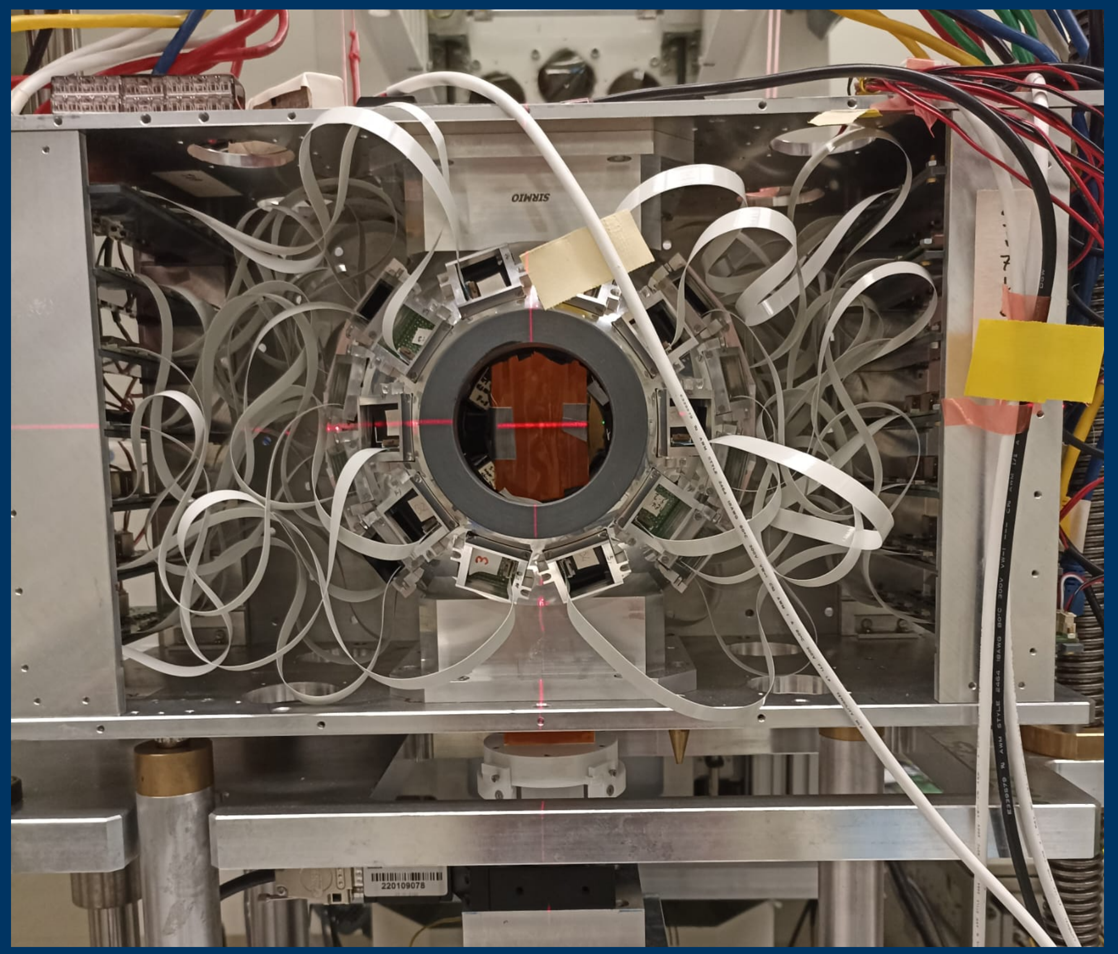




SIRMIO PET
Inner radius: 72 mm
Number of detectors: 56
Number of rings: 6
coverage: 44%

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN erc

PI: Katia Parodi



Daria Boscolo
Marco Durante

BARB Biomedical experiments

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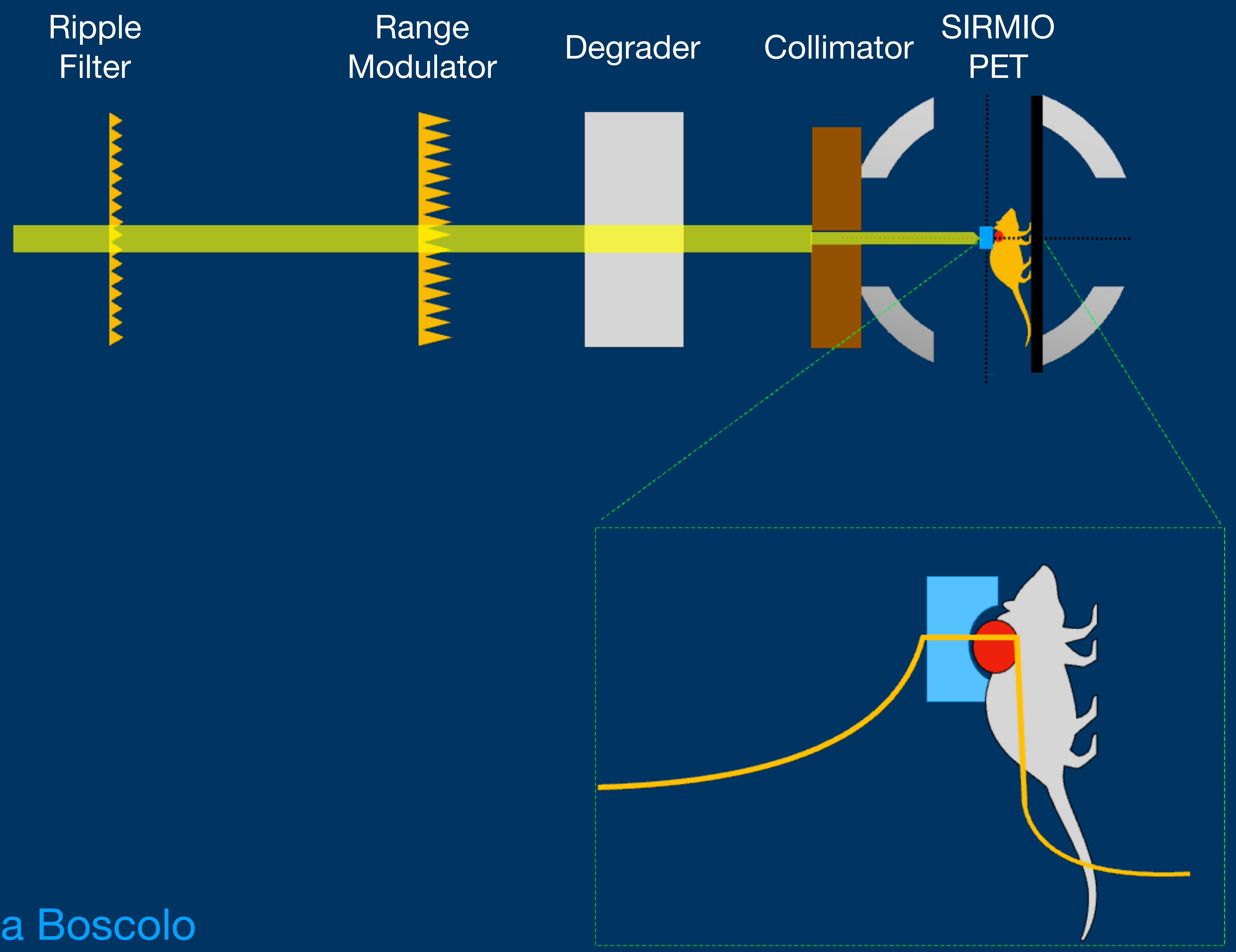
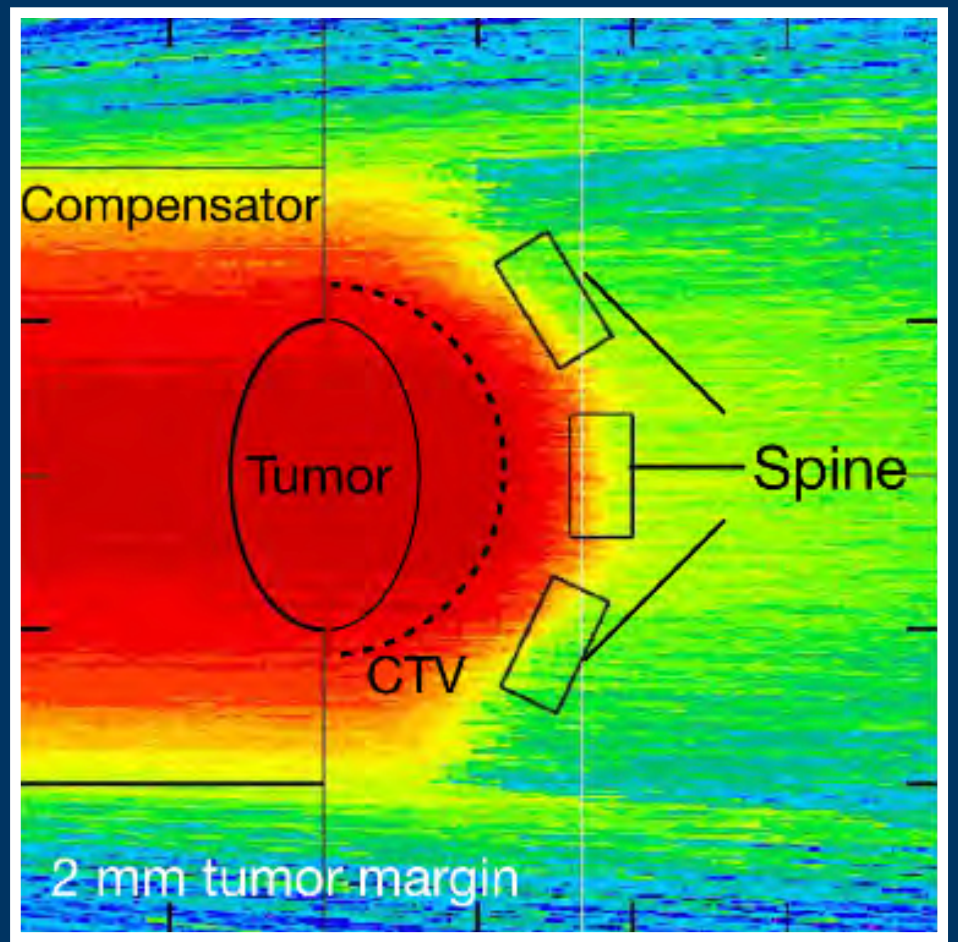
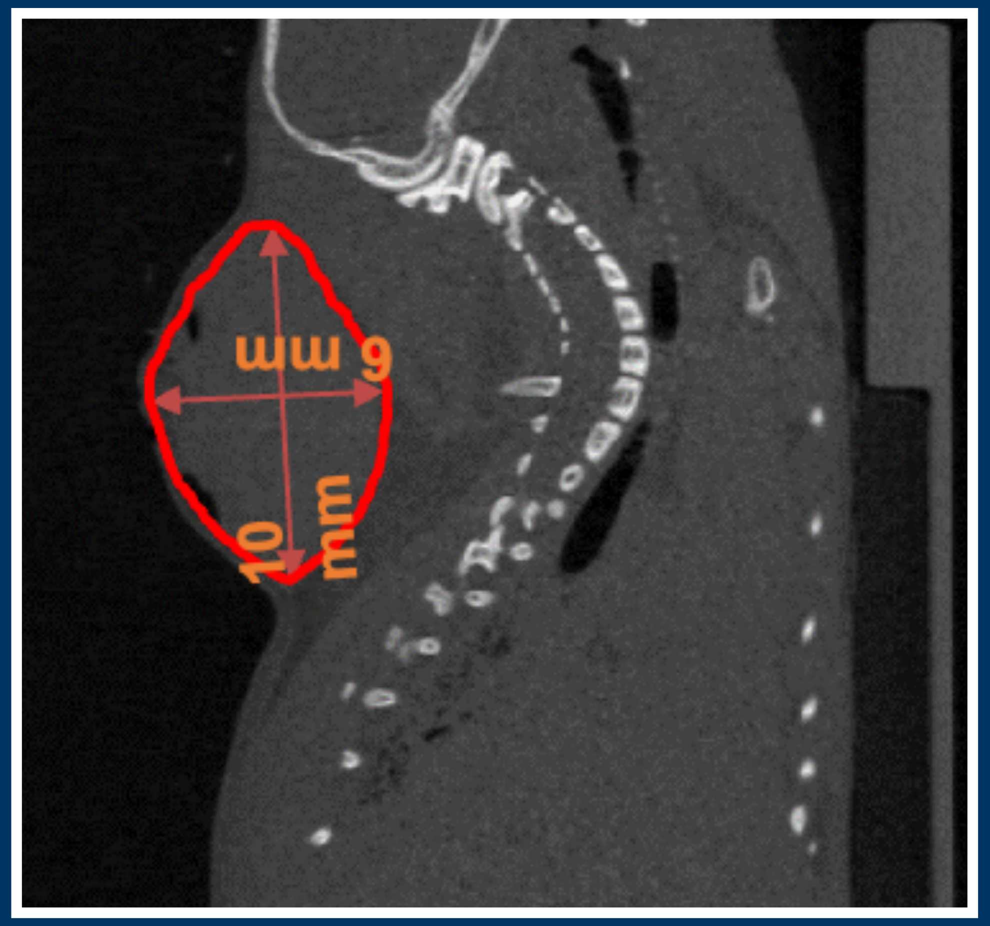


Pre-irradiation assessment

Monte Carlo simulation



CT



Beam

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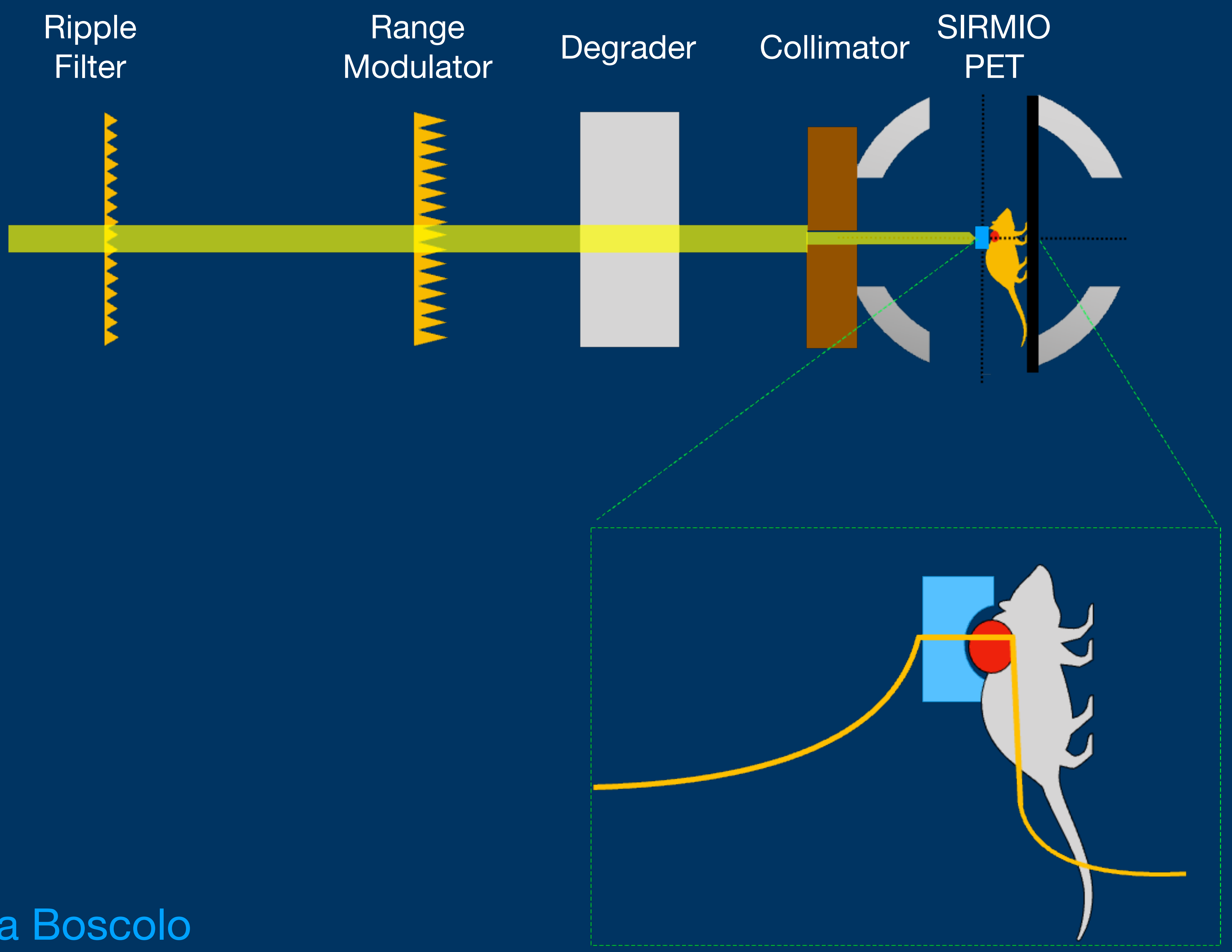
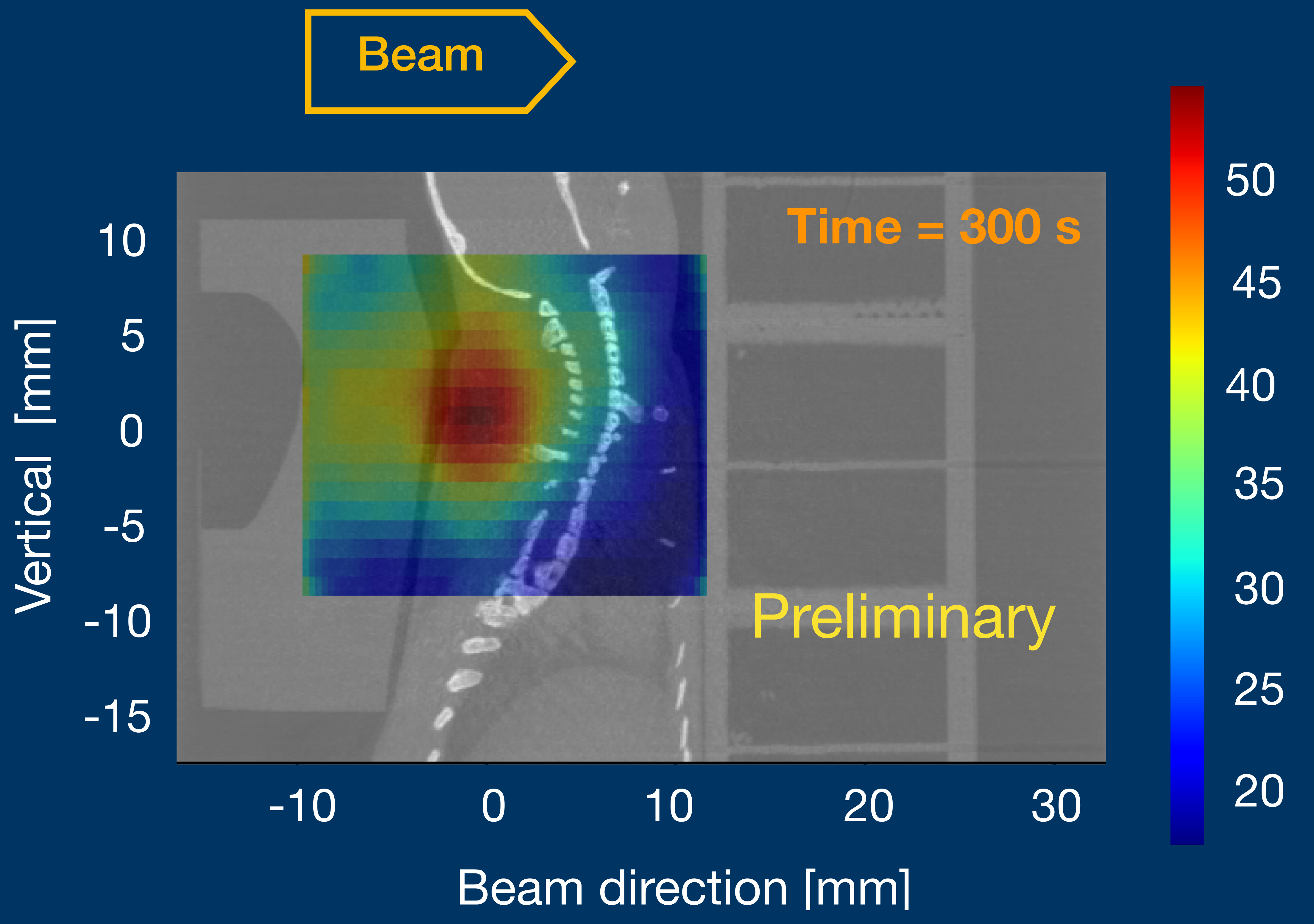
Marco Durante

BARB Biomedical experiments

Online PET imaging of the radioactive 11C while treating a tumour sparing the spinal cord





Daria Boscolo
Marco Durante

Conclusions and Outlook

- Therapeutic-quality 11C and 15O can be efficiently produced via the in-flight method, ensuring high intensities and purities.
- 15O stands out as the prime candidate for quasi-real-time range monitoring, offering significant advantages from an imaging standpoint.
- Successful transportation of Radioactive Ion Beams (RIBs) from the Fragment Separator (FRS) to the GSI medical cave (HTM) has been accomplished.
- Demonstrated success in small animal irradiation and imaging using 11C, indicating promising applications in preclinical research.
- Implementation of online imaging techniques for radioactive 11C during tumour treatment, effectively sparing critical structures like the spinal cord, has been achieved.

Acknowledgements

BARB Collaboration

Super-FRS Experiment Collaboration

GSI

FAIR Phase 0 Research Program

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Super-FRS EC

APPA

erc

B · A · R · B

LMU Ludwig-Maximilians-Universität München

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THANK YOU