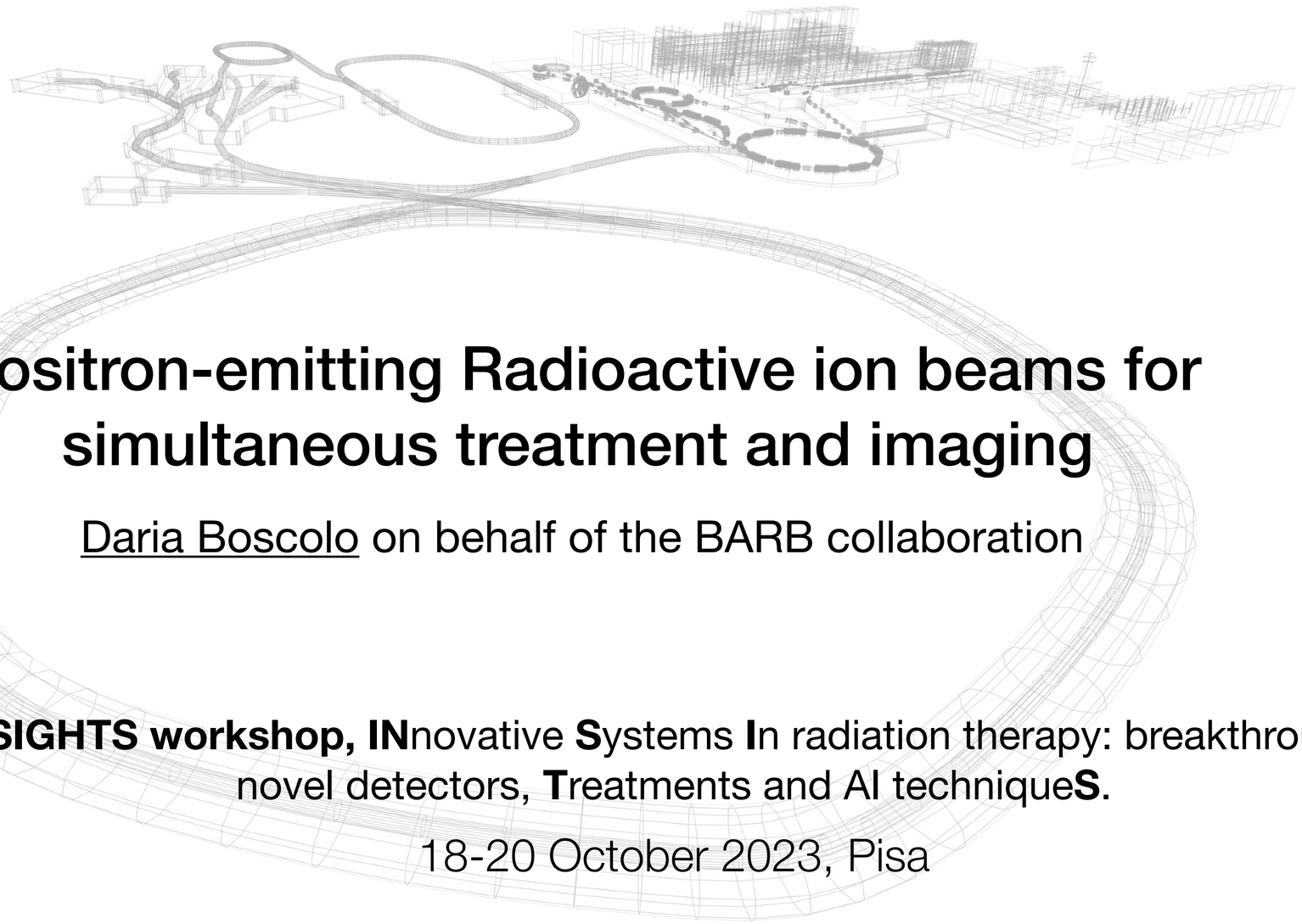


Positron-emitting Radioactive ion beams for simultaneous treatment and imaging

Daria Boscolo on behalf of the BARB collaboration

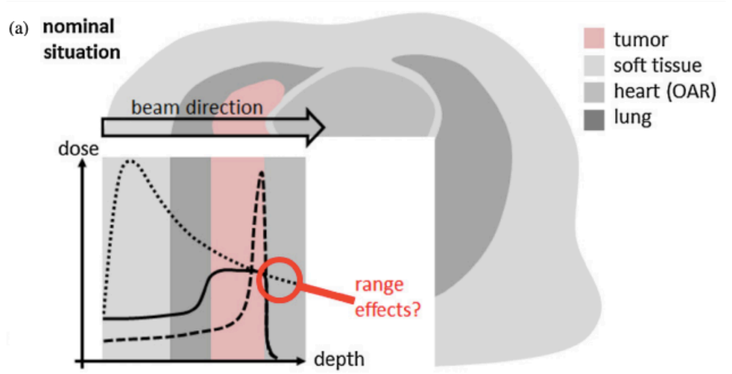
INSIGHTS workshop, INnovative **S**ystems **I**n radiation therapy: breakthrou**GH**s novel detectors, **T**reatments and AI techniqu**eS**.

18-20 October 2023, Pisa

Bragg peak and range uncertainty in radiotherapy

ION THERAPY IS A CORNERSTONE FOR TUMOR TREATMENT

- defined range and Bragg peak —> spare normal tissues



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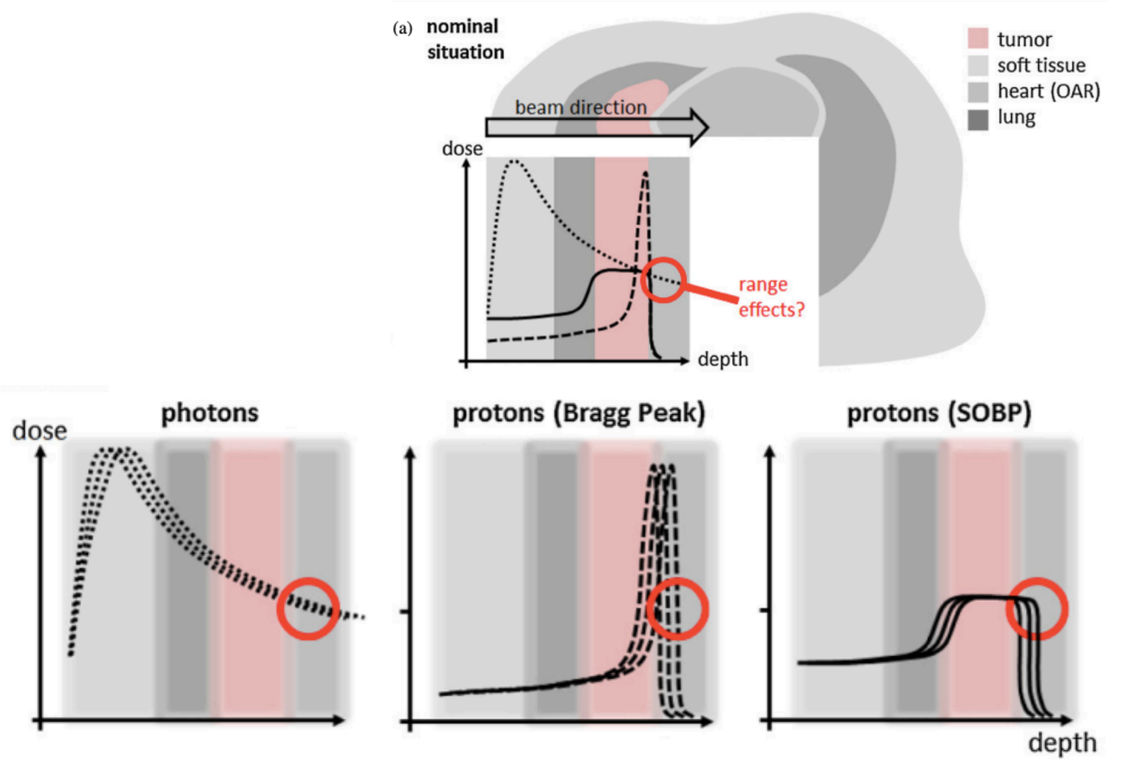
RANGE UNCERTAINTY

- Uncertainties in conversion of CT numbers to stopping power
- Quality of the CT
- Daily errors: patient setup and alignment, tumor shrinkage, anatomical changes…



Knopf & Lomax, Phys Med Biol 2013

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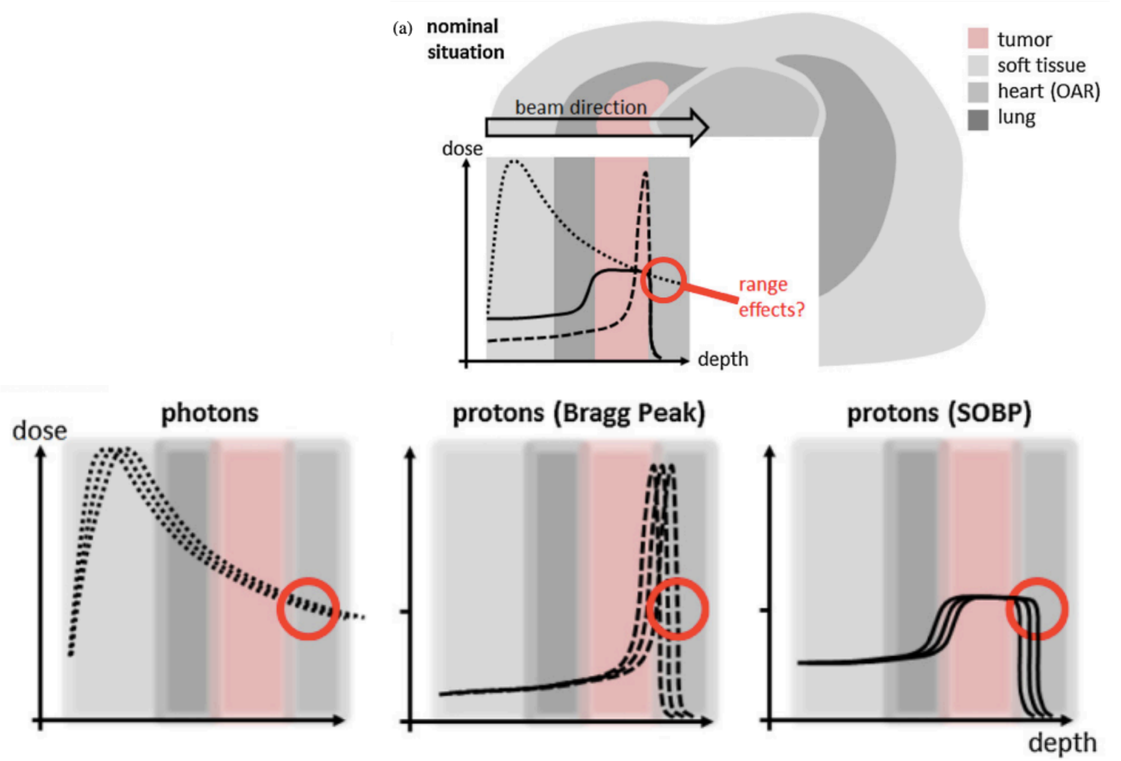
- Daily errors: patient setup and alignment, tumor shrinkage, anatomical changes…

Margins have to be added to ensure tumor coverage

- **Advantage of Bragg peak is jeopardized**
- **More damage to normal tissue**

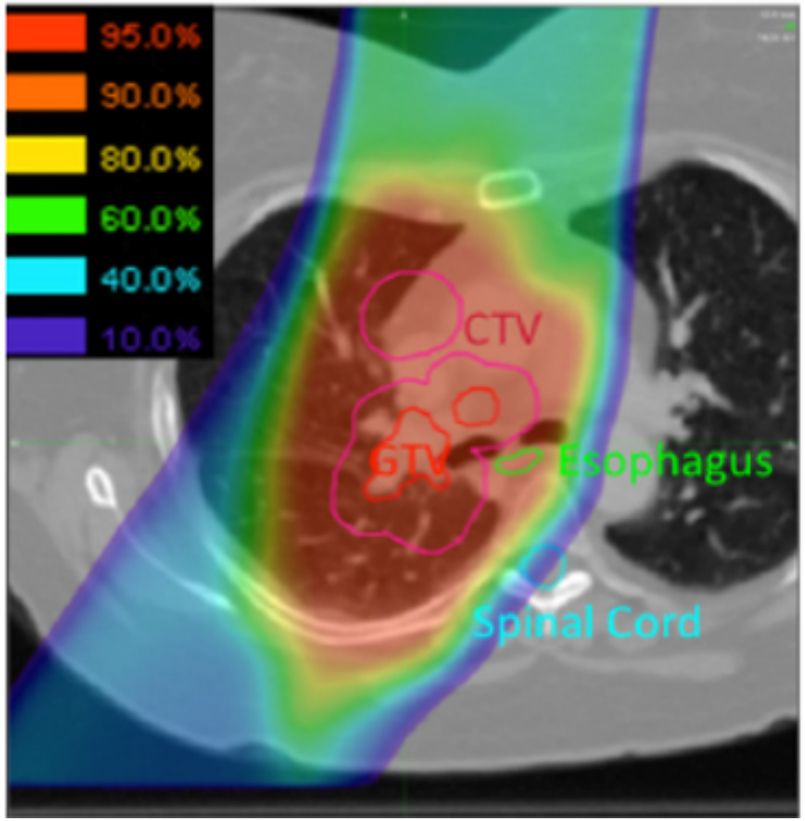


Knopf & Lomax, Phys Med Biol 2013

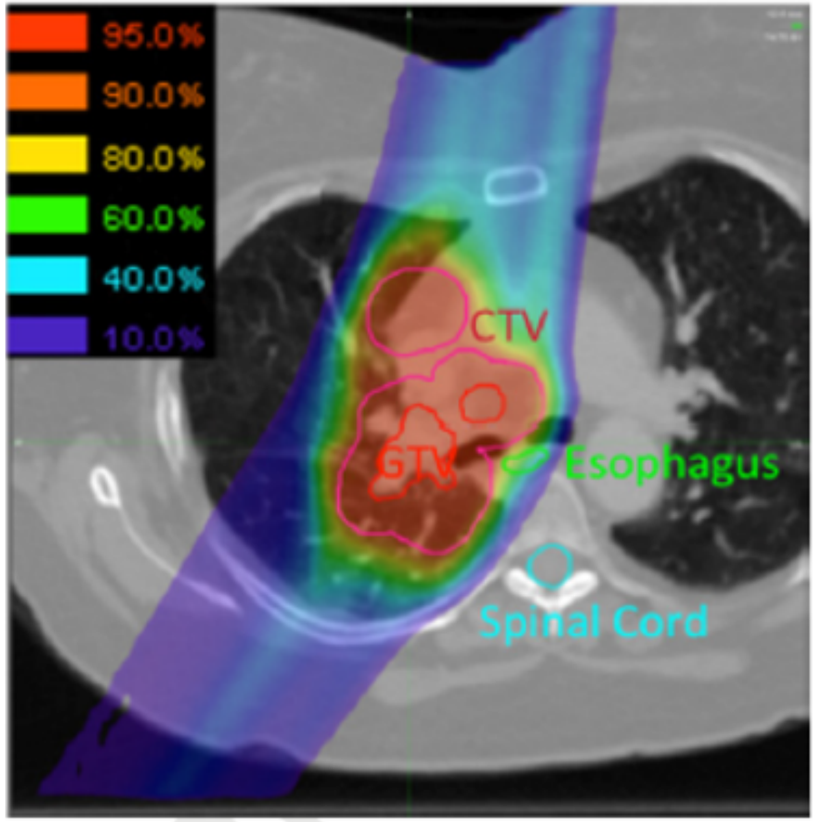
Dose conformity w/wo margins

Proton treatment: Dose distribution created in proton therapy vs what can be achieved from the physics point of view

Proton treatment plan with margin ~1 cm (in total)

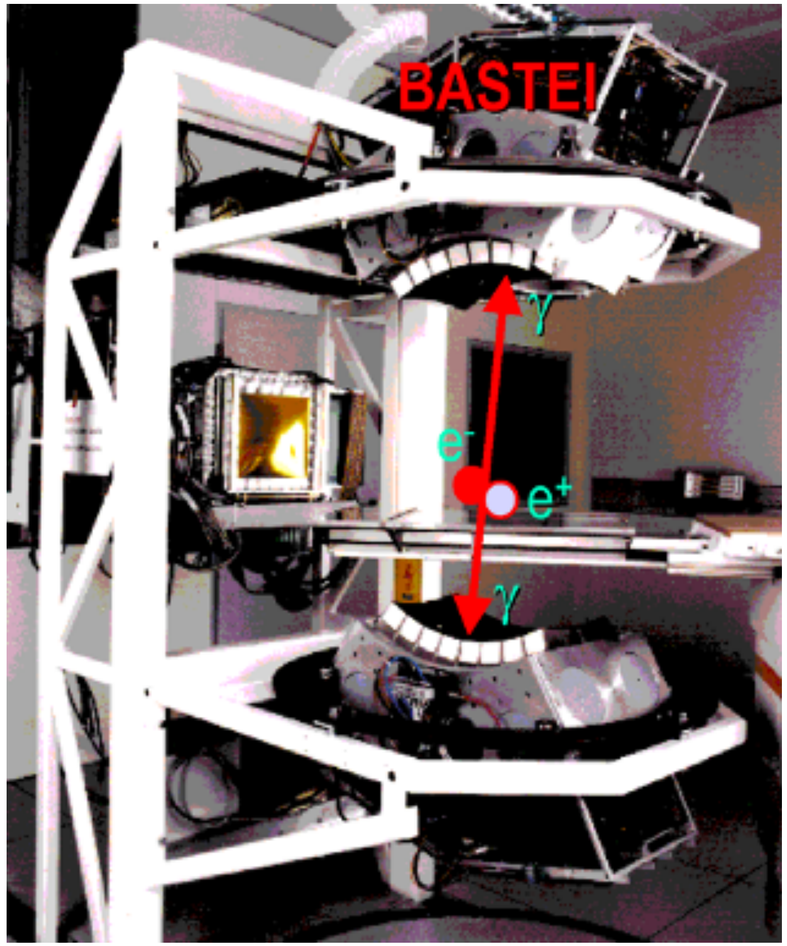


Proton treatment plan No margin (proton penumbra ~2 mm)



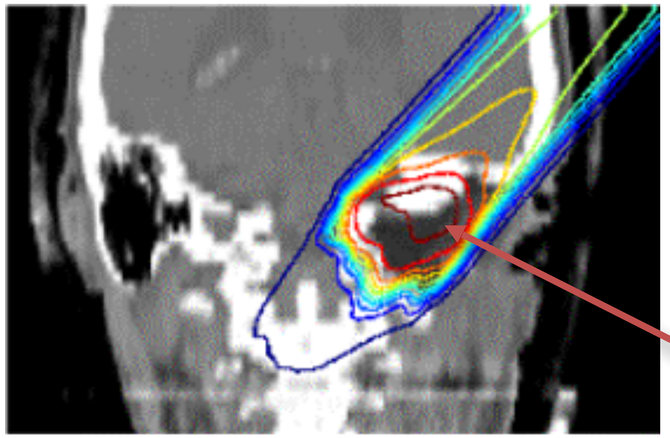
Durante & Flanz, Semin. Oncol. 2019

Beam monitoring with PET: ^{12}C

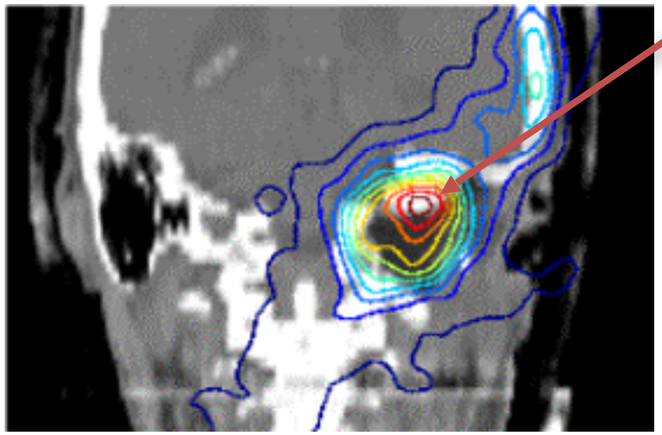


BASTEI system at GSI

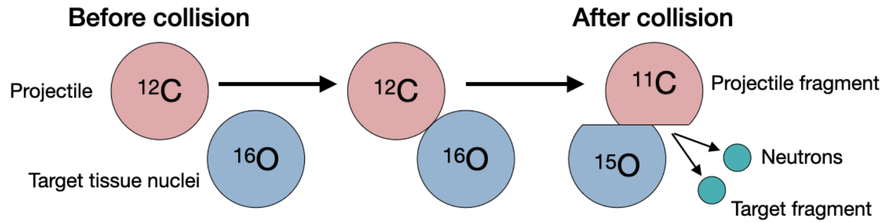
DOI: 10.1007/BF03038884



Planned dose distribution



Measured β^+ activity



Shift between the peaks

\+ too long half-life of the most abundant induced radionuclides

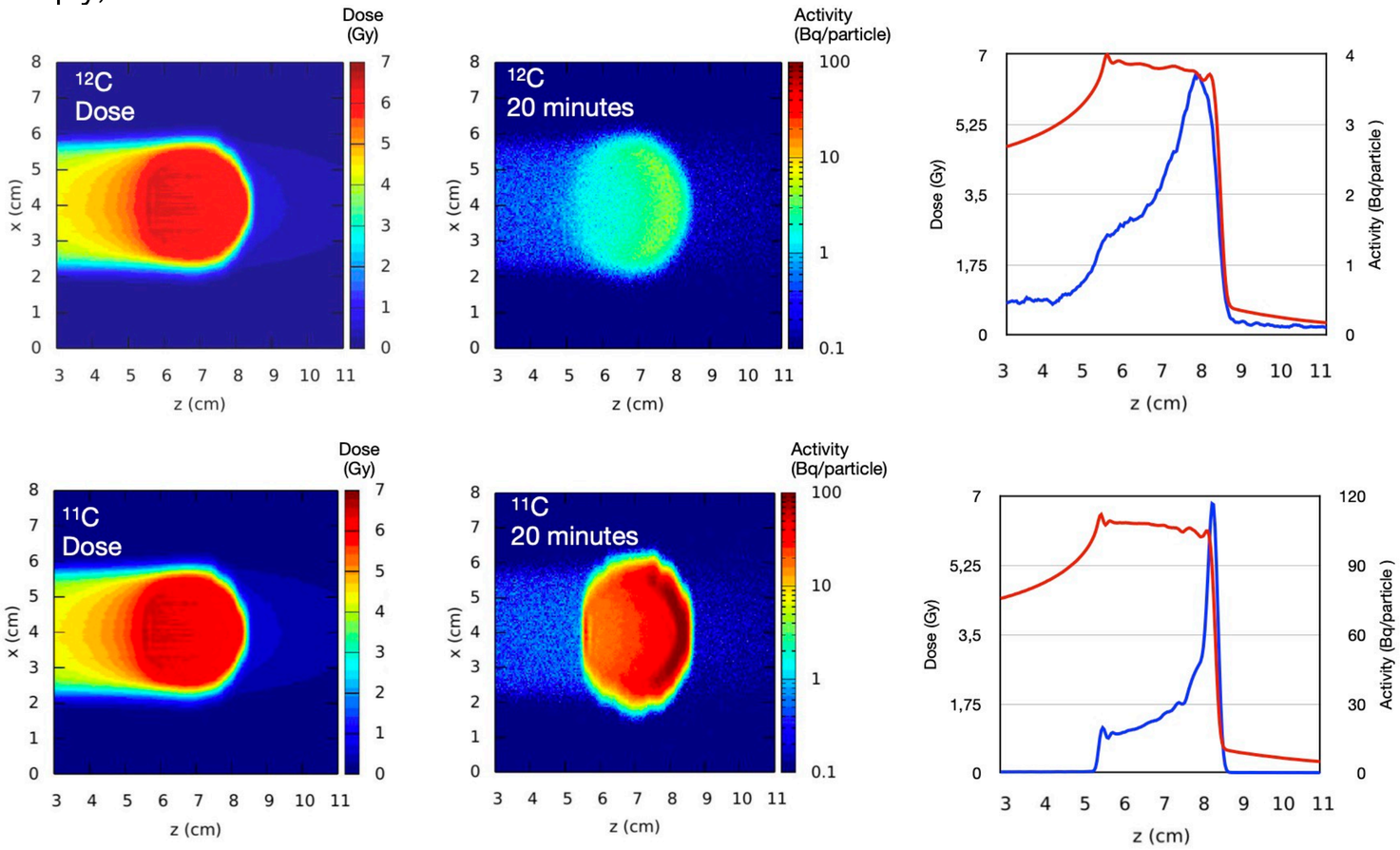
Courtesy of Wolfgang Enghardt, HZDR, Dresden

Radioactive Ion Beams (RIB) for simultaneous treatment and range verification

Respect to conventional PET imaging in heavy ion therapy, RIBs show:

- Improved count rate (one order of magnitude larger than for stable ions)
- Improved correlation between activity and dose
- Reduced washout blur thanks to short lived isotopes

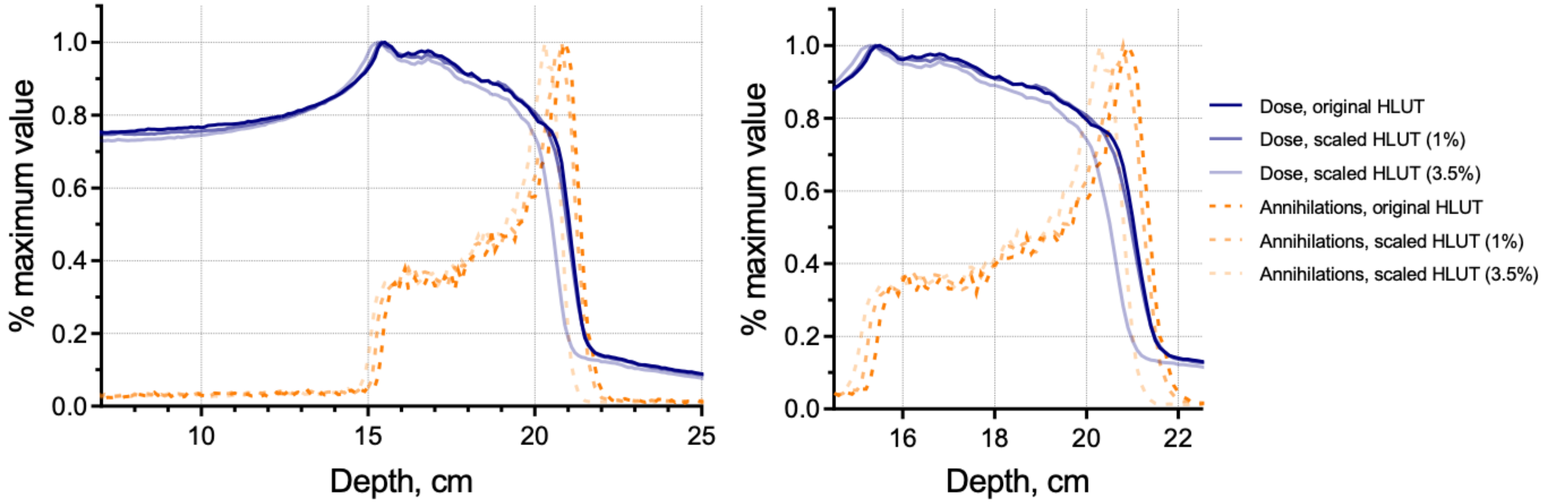
The challenging production and the difficulties in reaching high intensities have discouraged the clinical application of RIB.



D. Boscolo, D. Kostyleva, M. J. Safari, V. Anagnostatou, J. Äystö, S. Bagchi, T. Binder, G. Dedes, P. Dendooven, T. Dickel, O.Sokol al., Front. Oncol. 11 (2021)

What can we gain with reduced margins?

TRiP98 treatment planning + FLUKA simulations:
Activity maps can <u>in theory</u> reflect the sub-mm shifts in dose distributions



Sokol et. al. Scientific Reports 2022

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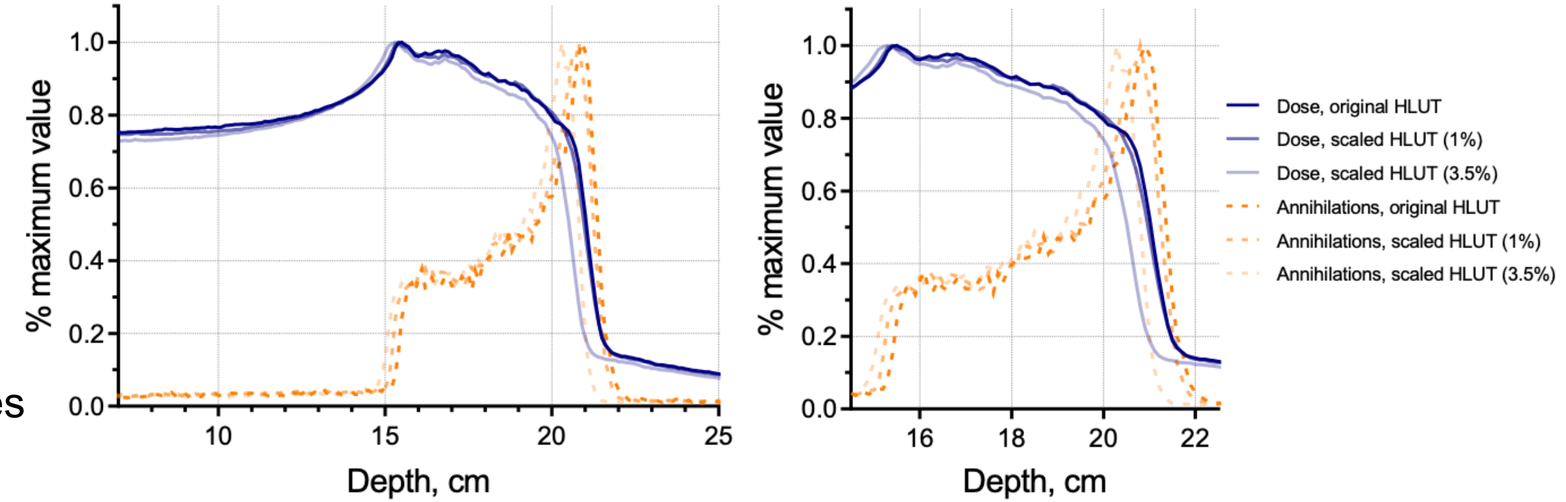
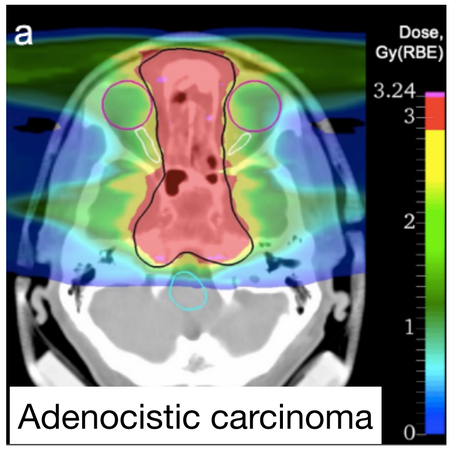
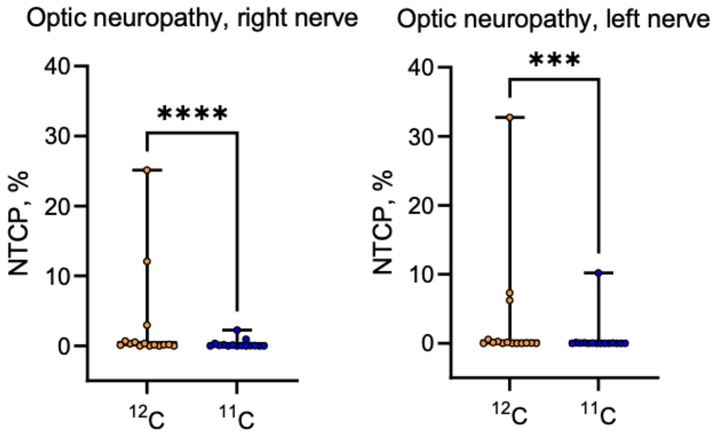


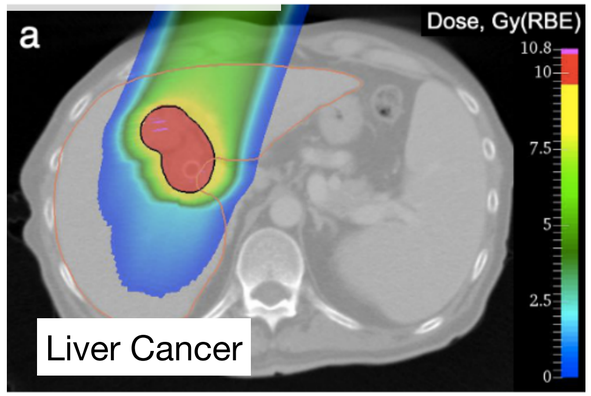
- Robust treatment planning
- ^{12}C: ± 3.5% range and ±3 mm setup uncertainties
- ^{11}C: only setup uncertainties

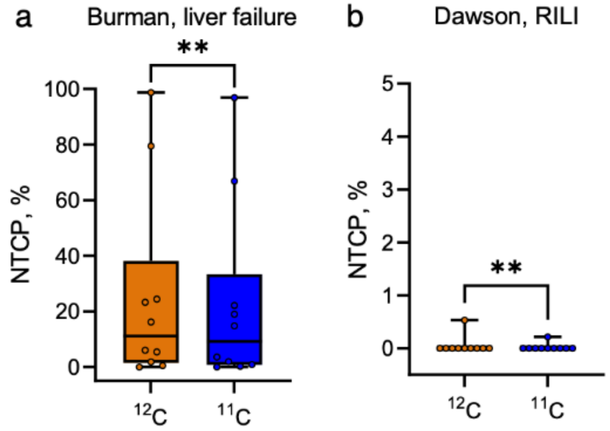
Serial OAR





Parallel OAR



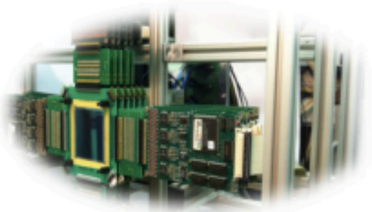
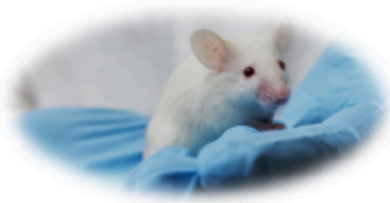
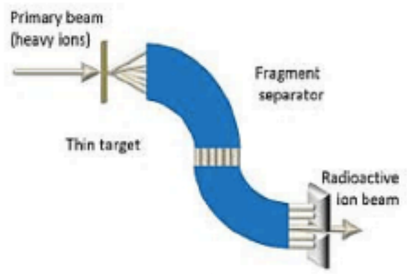
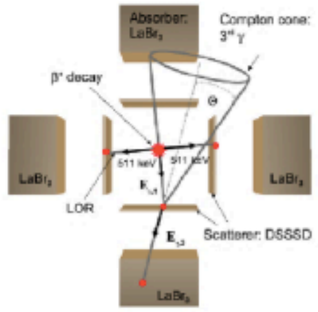
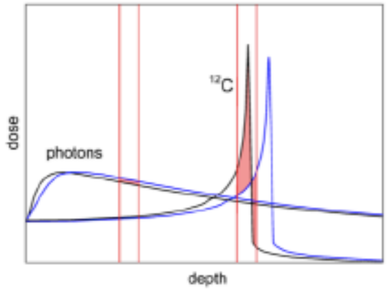
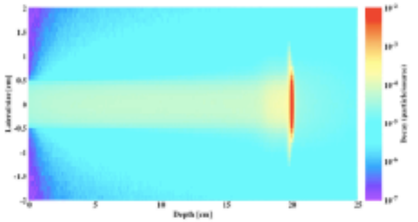


Significant NTCP reduction for both serial and parallel OAR

Sokol et. al. Scientific Reports 2022

The BARB project: biomedical application of radioactive ion beams

B • A • R • B
BIOMEDICAL APPLICATIONS OF RADIOACTIVE ION BEAMS

OBJECTIVES	Measure maximum achievable intensity for ^{12}C- and ^{16}O-derived RIB	Design hybrid γ-PET detector superior to state-of-the-art PET	Select best high-intensity RIB for therapy	Define maximum accuracy and resolution for RIB CPT	Validate therapeutic potential of RIB in animals
					
METHODOLOGY	Produce light RIB using fragment separator at FAIR	Development of hybrid γ-PET detector through collaboration with LMU	Conduct biophysical dosimetric studies in phantoms and mammalian cells	Visualize RIB using BASTEI PET camera and hybrid γ-PET detector	Assess tumour growth post-irradiation in soft-tissue sarcoma model
					
OUTCOMES	**Production of high-intensity RIB for first-time therapeutic use**	**Real-time imaging and monitoring of high-intensity RIB**	**Identification of RIB suitable for therapeutic applications**	**Unprecedented imaging accuracy for therapeutic beam delivery**	**Improved precision of RIB CPT for cancer and other indications**

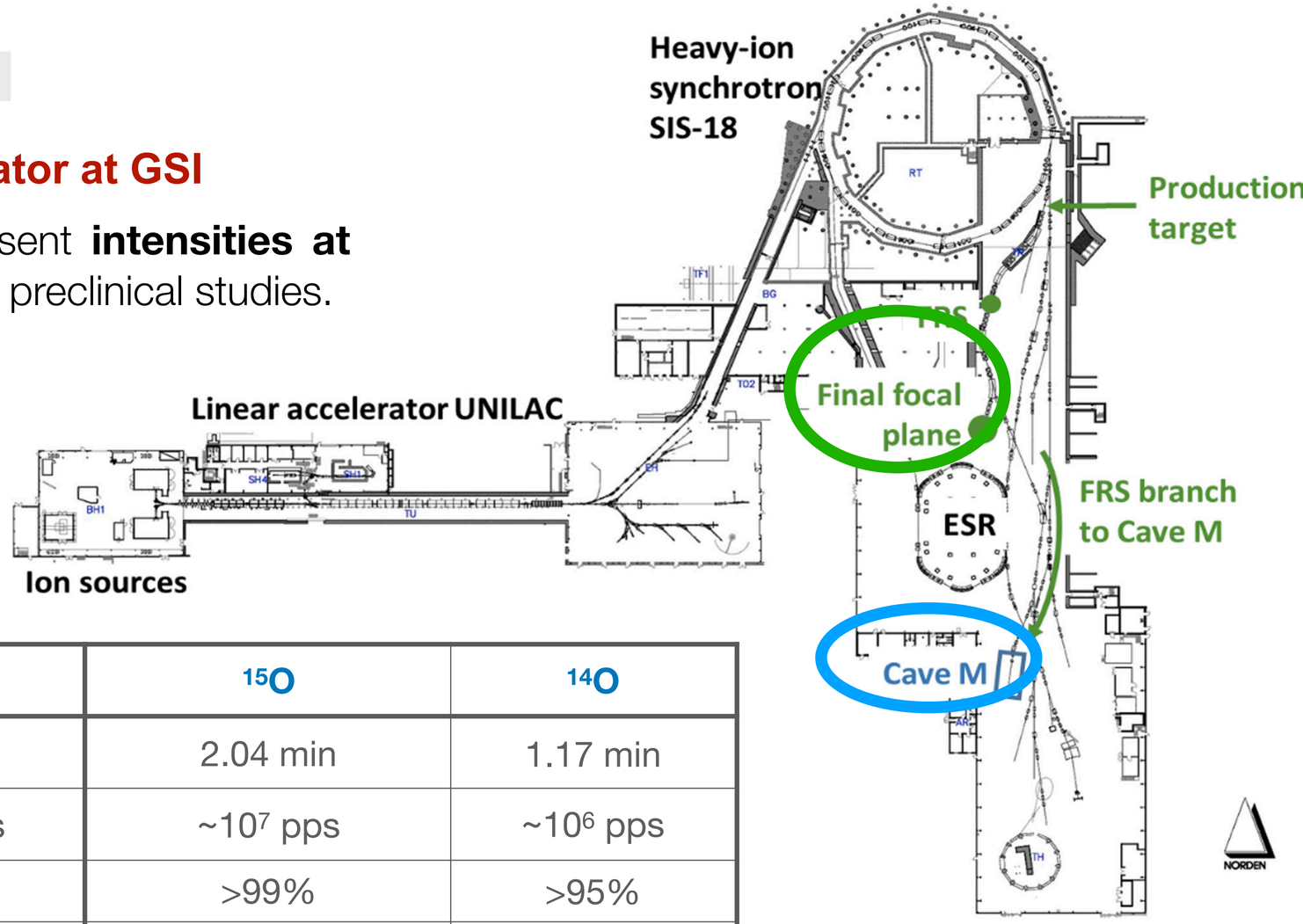
https://www.gsi.de/work/forschung/biophysik/erc_barb

erc European Research Council

RIBs at GSI-FAIR

FAIR Phase 0: upgrade of the SIS-18 accelerator at GSI

With the **fragment separator FRS** and the present **intensities at the SIS18** it is possible RIB intensities sufficient for preclinical studies.

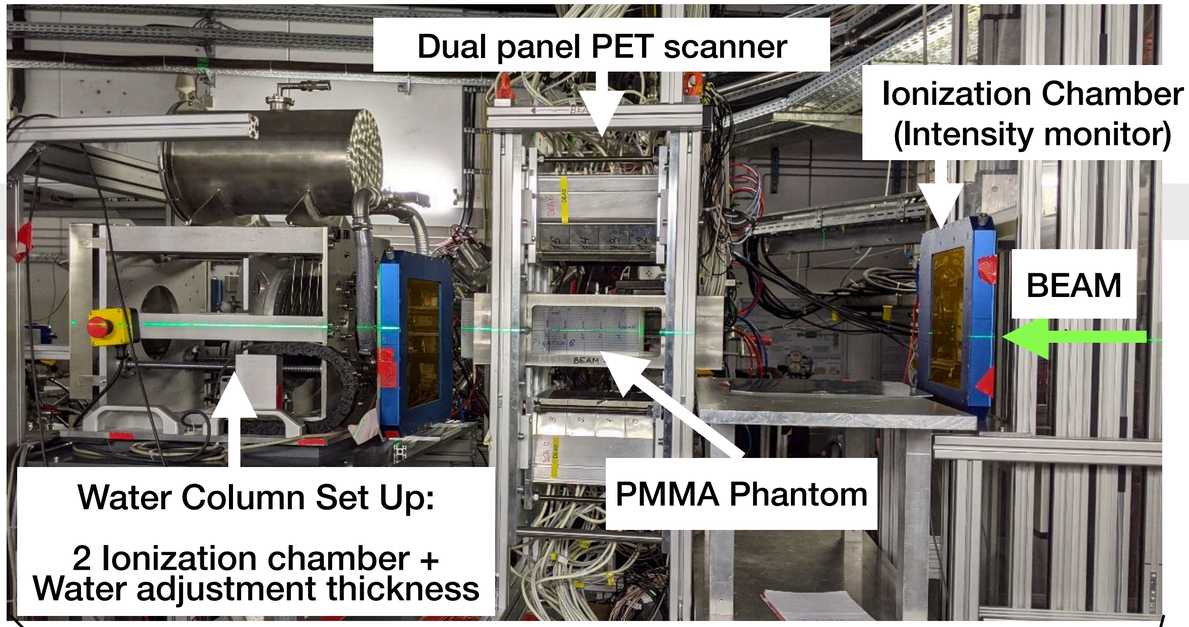


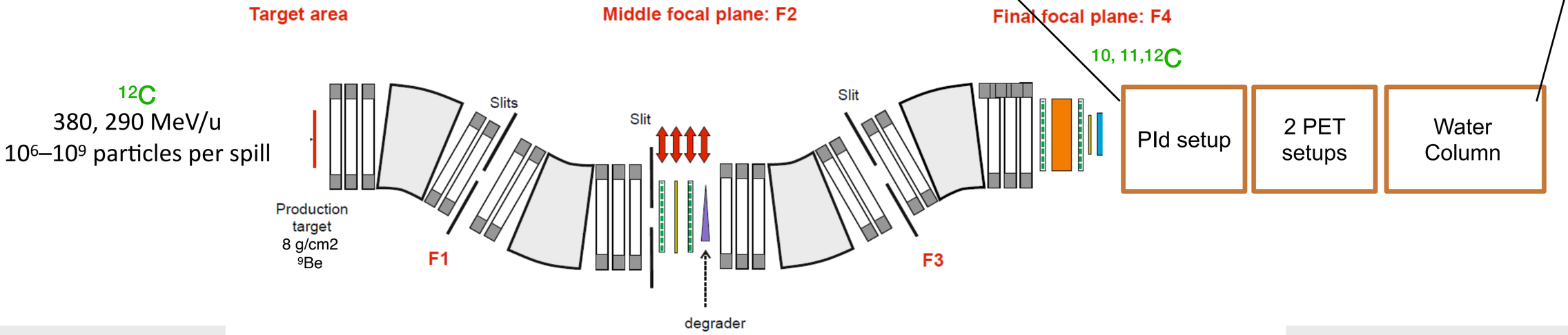
RIBs used in the BARB project:

Isotope	^{11}C	^{10}C	^{15}O	^{14}O
Half-life, min	20.4	19.3 s	2.04 min	1.17 min
Intensities	~10^7 pps	~10^6 pps	~10^7 pps	~10^6 pps
Purity	> 99%	> 94%	>99%	>95%
Energy:	- 146 MeV/u - 258 MeV/u	- 155 MeV/u - 272 MeV/u	-285 MeV/u -185 MeV/u	-320 MeV/u -192 MeV/u
Extraction point	final focal plane FRS	final focal plane FRS	**Cave M** final focal plane FRS	final focal plane FRS

Carbon isotopes: Experimental set up

- Iso- range ^{11}C and ^{10}C beams were produced in flight extracted at the final focal plane of the FRS.
- The beams have been characterised and implanted in Plastic phantoms for PET images acquisition.
- Different beam optics were tested to select the best beam for preclinical applications.





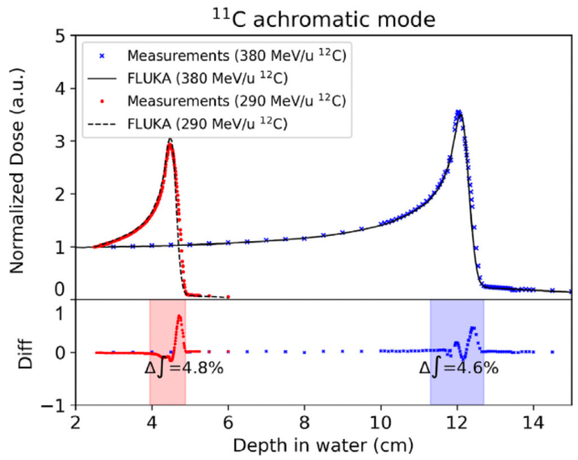
Carbon isotopes: Beam characterization

For all the Carbon isotopes the beam was characterized with the standard FRS setup and the Water column set up, in terms of:

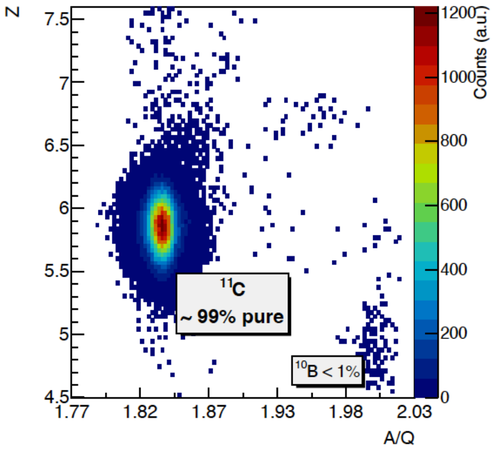
- **Particle identification**
- **momentum spread**
- **beamspot size and divergence**
- **Bragg curves and ranges in water**

^{11}C 258 MeV/u achromatic mode

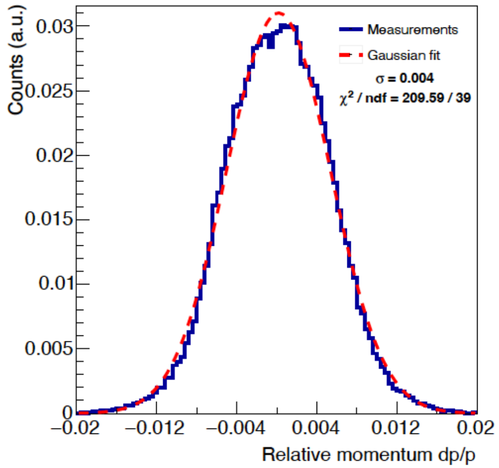
Bragg Curves and ranges in water



Particle identification



Momentum Spread



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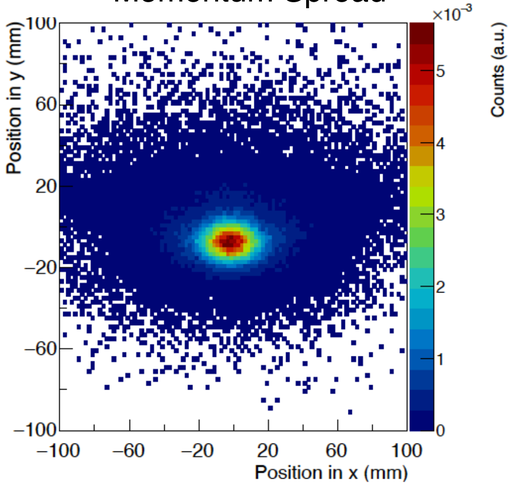
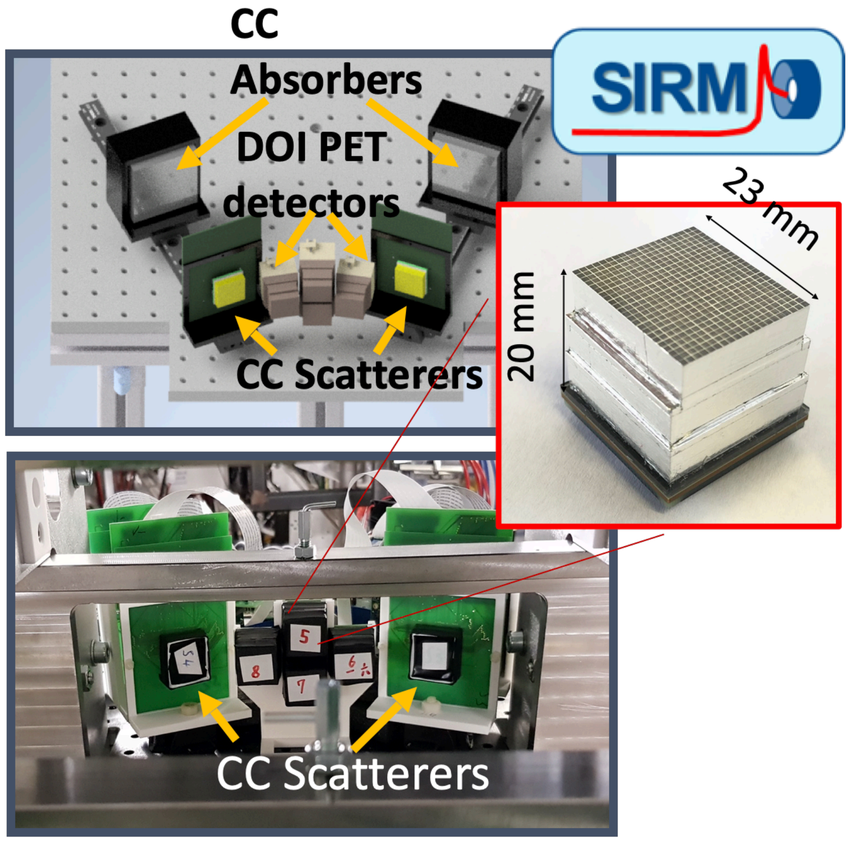


Boscolo et al. NIM A 2022

Imaging: LMU PET-Compton hybrid detector



Prototype of LMU-PET detector:

- components testing of the **In-beam small animal hybrid PET-Compton SIRMIO-BARB detector** (www.lmu.de/sirmio)
- *3-layer scintillator block, a light guide and an 8x8 SiPM array*
- **High spatial resolution < 1 mm**
- In collaboration with NIRS-QST (T. Yamaya and H.G.Kang).

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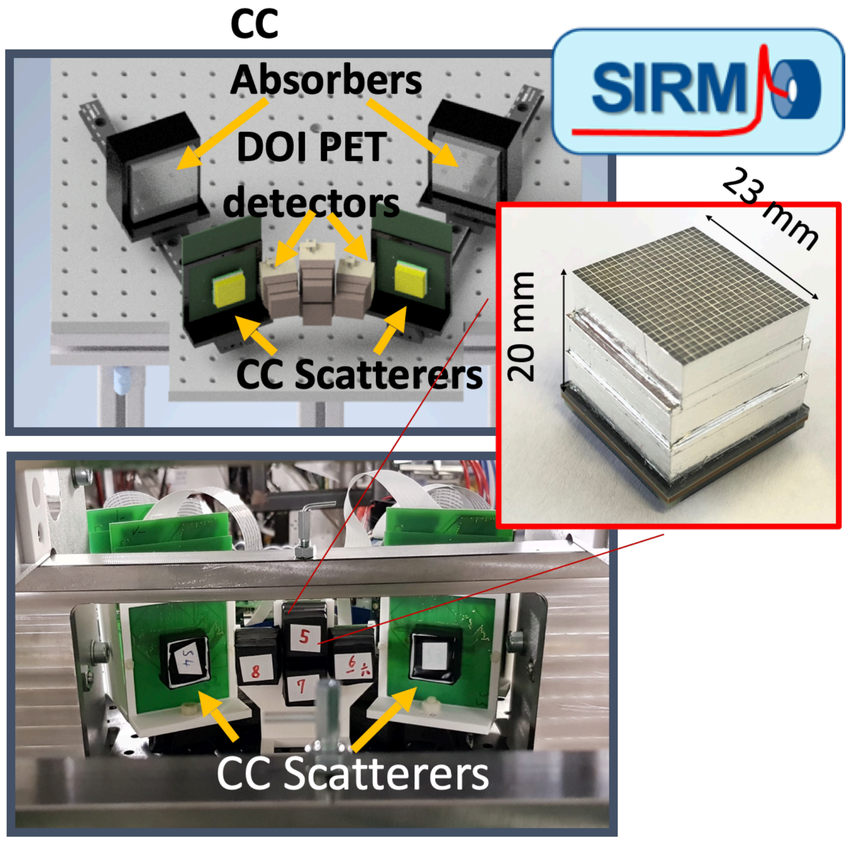

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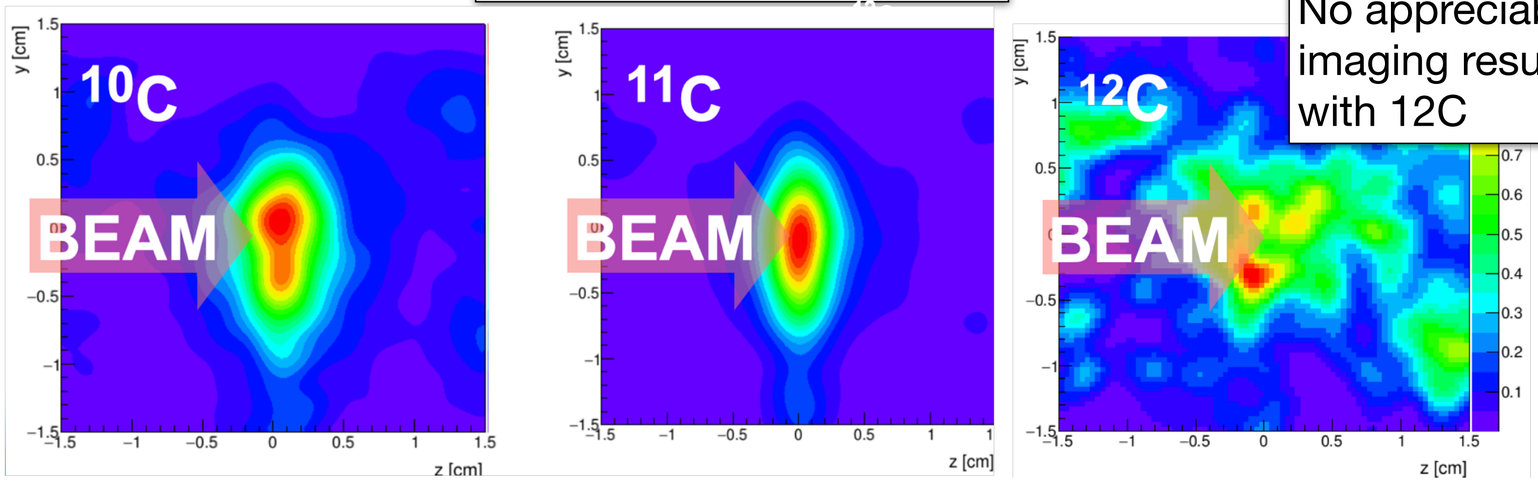
Mono-energetic mode

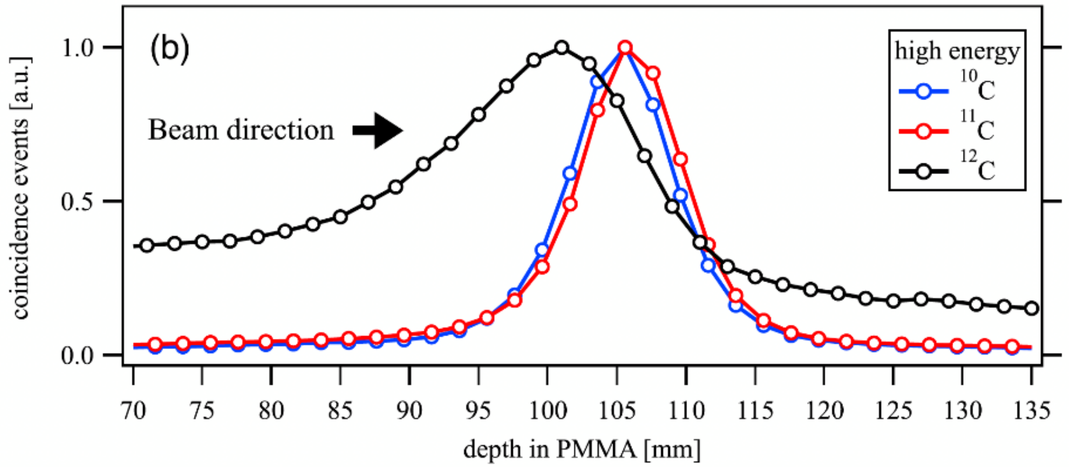


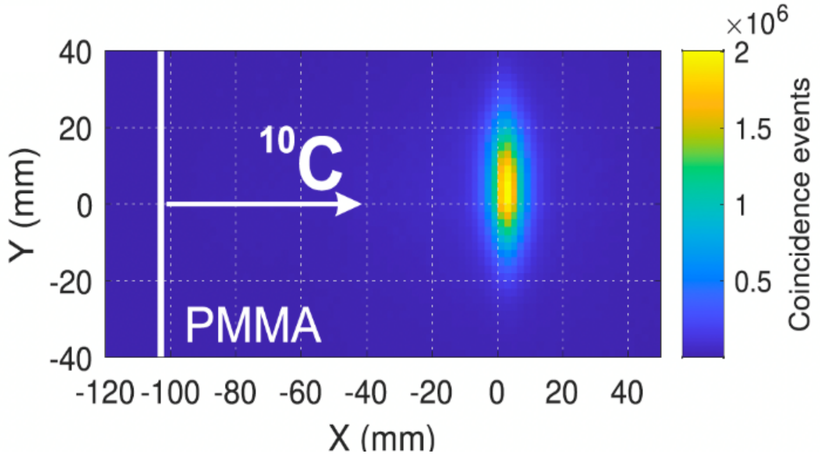
No appreciable imaging results with 12C

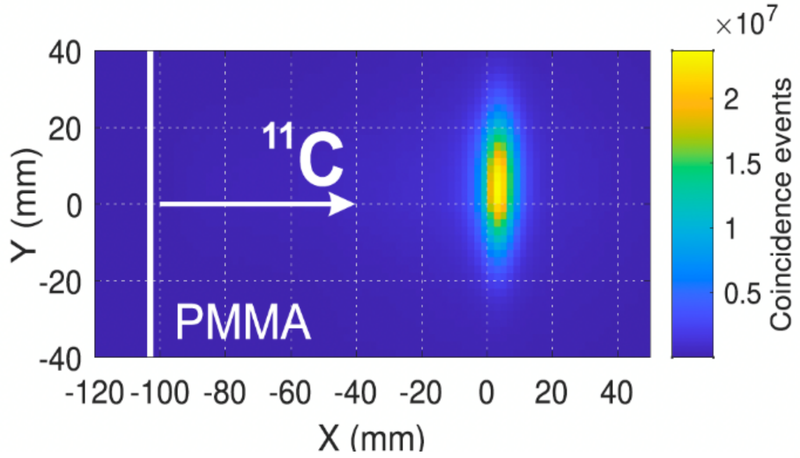
Courtesy of Giulio Lovatti, LMU

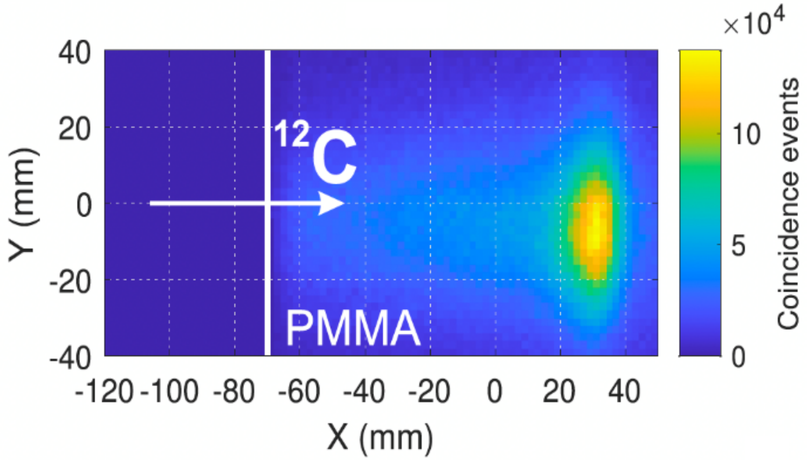
Imaging: UMCG dual-panel imaging system

- 1/6 of a Siemens Biograph mCT clinical PET scanner with custom-modified detectors.
- Two detector panels installed above and below the phantom each at a distance of 30 cm
- RIB stops in the PMMA phantom







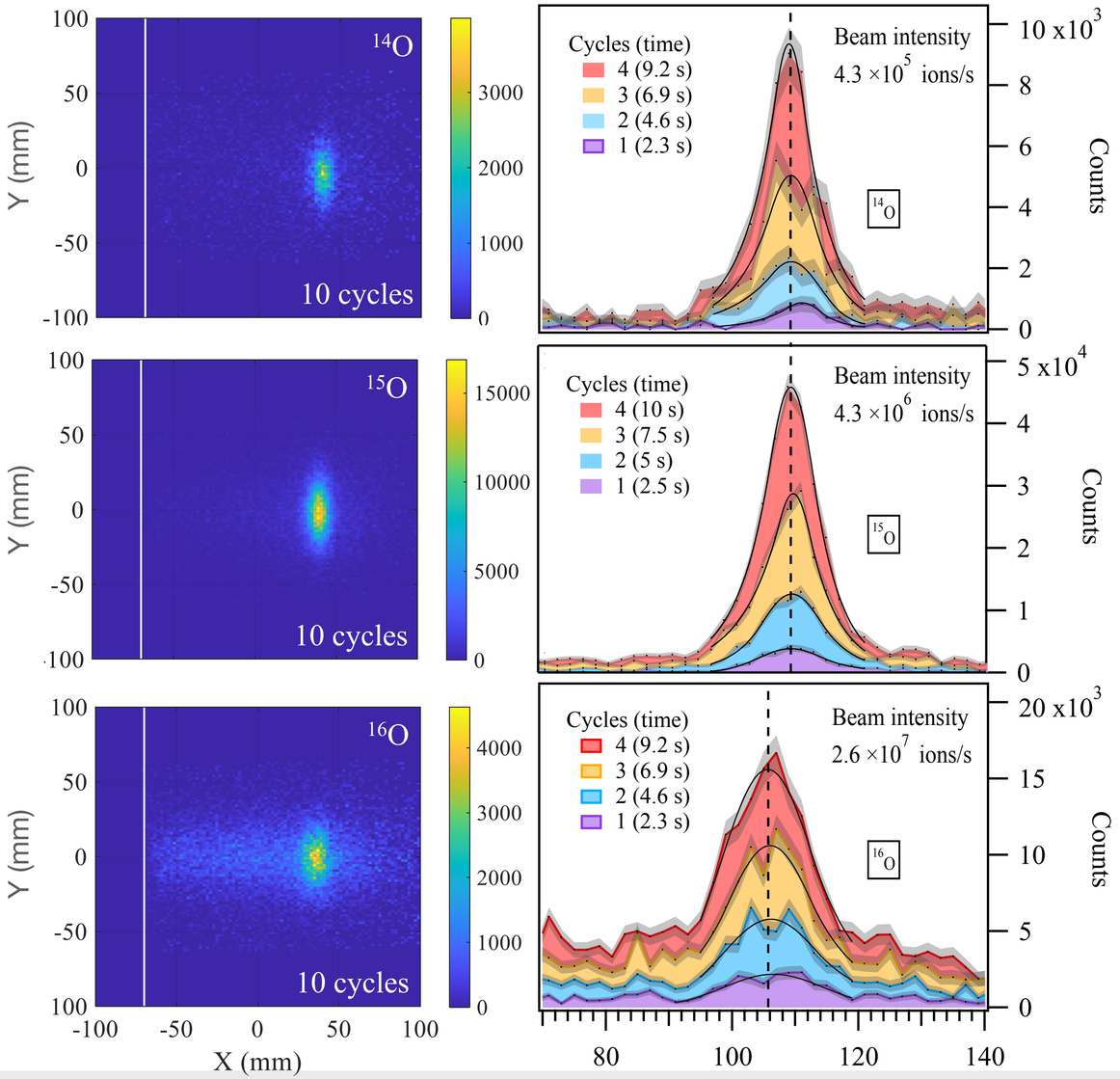


PET range uncertainty after delivering 1.6 x 10^7 ions in 4 spills (19.2 s total): 0.04 mm, 0.7mm, and 1.3 mm for ^{10}C, ^{11}C, and ^{12}C

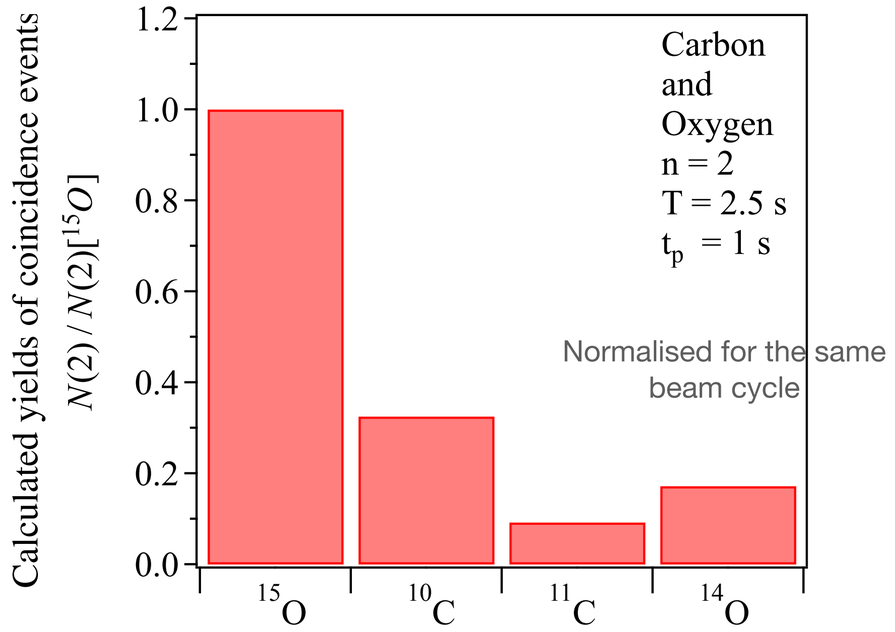
Kostyleva et al. Phys. Med. Biol. 2022

More in Peter Dendooven talk this afternoon…

First experiments: ^{15}O and ^{14}O @ the FRS



^{15}O best performing RIB for quasi-real-time range monitoring

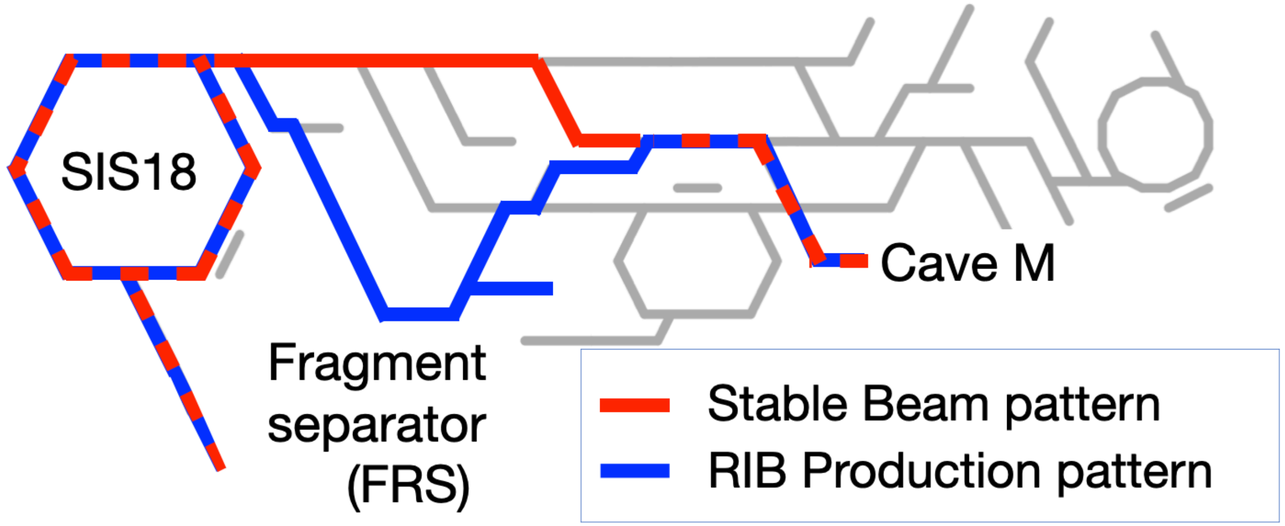


- ^{11}C —> longer half life
- ^{10}C and ^{14}O —> lower production rates (low intensities)

More in Peter Dendooven talk this afternoon…

Purushothaman et al. accepted Scientific Report

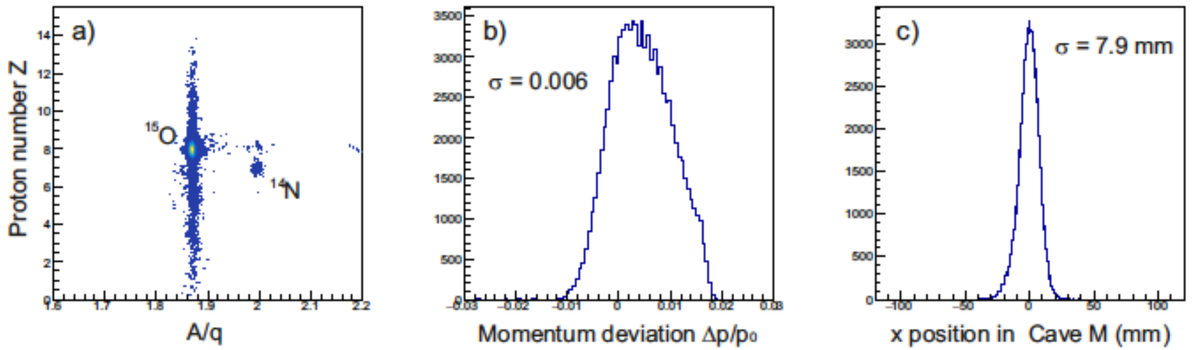
First experiments: ^{15}O in Cave M



Isotopes:	^{15}O
Half-life:	2.04 min
Intensities	~10^7 pps
Purity	>99%
Energy:	285 MeV/u
Extraction point	**Cave M**
Transmission SIS18->CaveM	**6E-04**
Transmission FRS ->Cave M	**6 %**

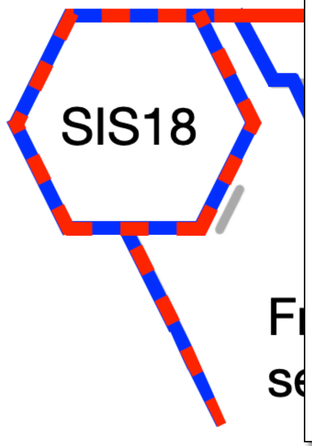
Cave M is the medical room @ GSI:

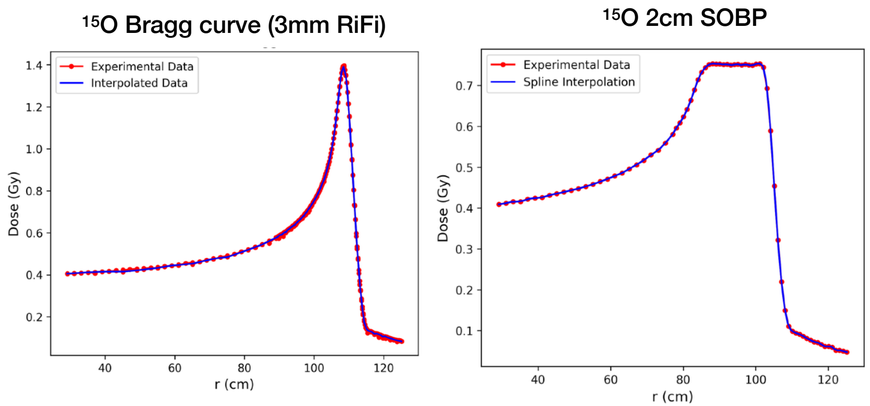
- Possibility to use raster scanner
- Possibility to use the standard nozzle for beam monitoring
- Possibility to use treatment planning softwares



E.Haettner et al. NIMB, 2023

First experiments: ^{15}O in Cave M



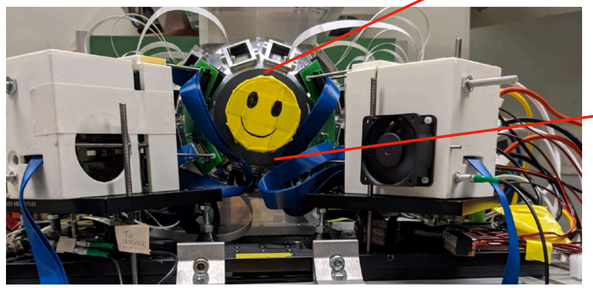


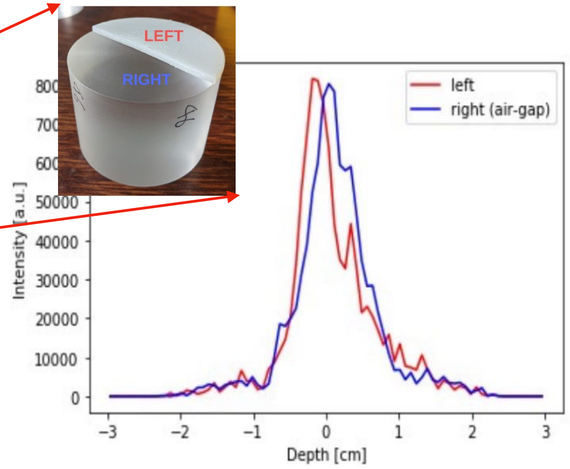
- Extended target irradiadiations with RIB have been performed

^{15}O
2.04 min
~10^7 pps
>99%
285 MeV/u
Cave M
6E-04
6 %

Cave M is the m

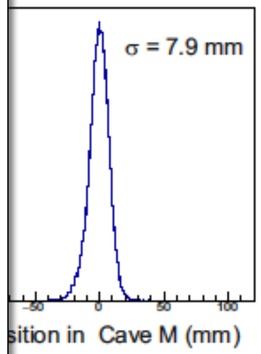
- Possibility to
- Possibility to
- Possibility to





- Prototype of the full SIRMIO PET detector.
- RIB PLASTIC phantom

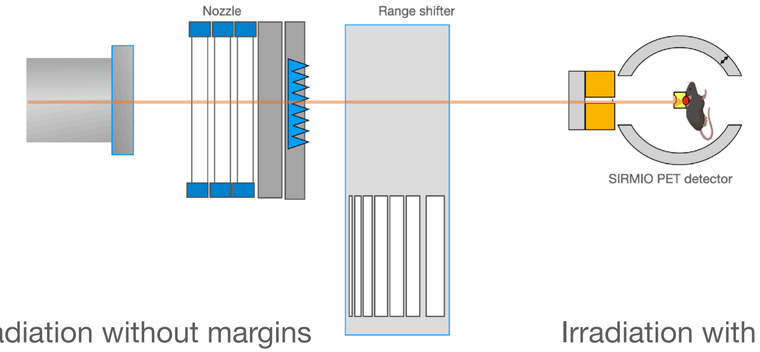
PET Images courtesy of Munetaka Nitta, Giulio Lovatti, Tim Binder, Marco Pinto, Vasiliki Anagnostatou, George Dedes, Peter Thirolf, Katia Parodi



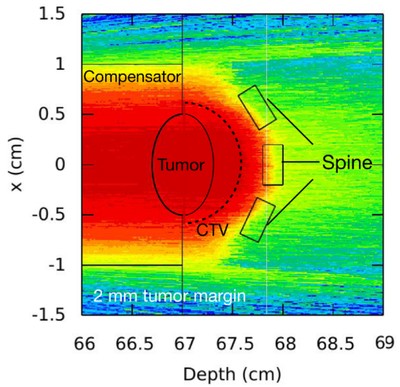
E.Haettner et al. NIMB, 2023

Planned Experiments February 2024:

Preclinical assessment of the advantages of online imaging using RIB

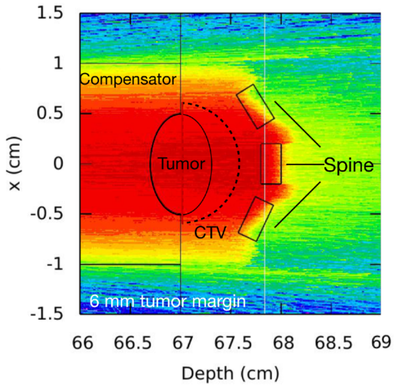


Irradiation without margins



FLUKA Simulations

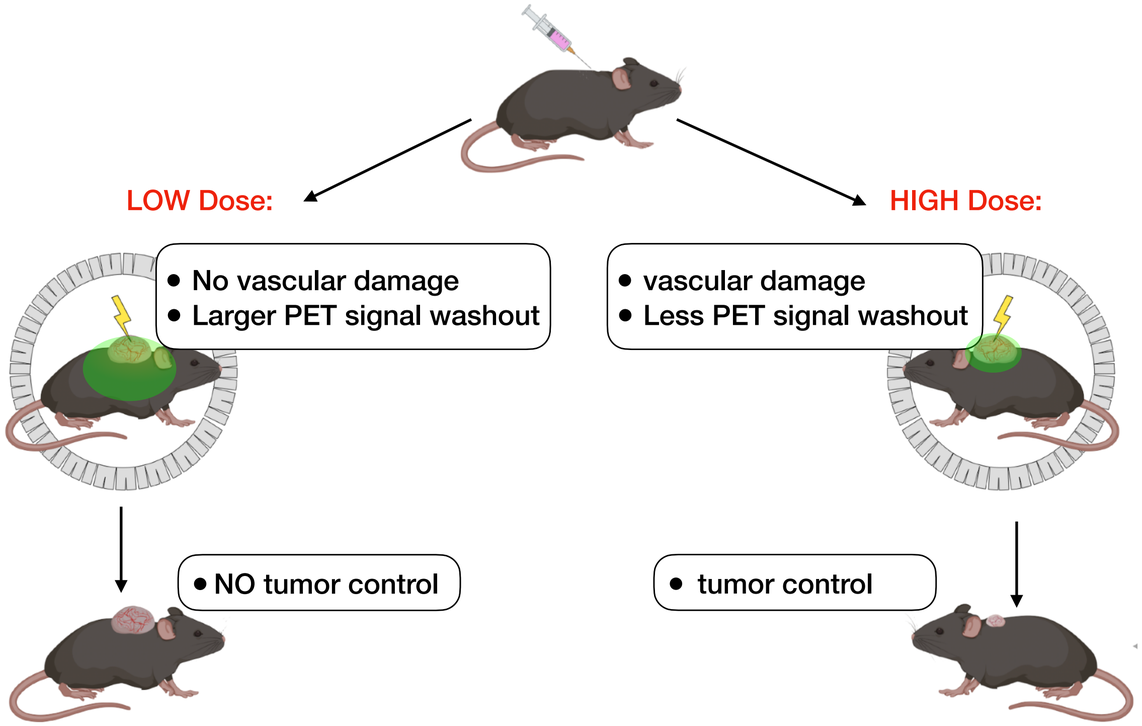
Irradiation with margins



Expected outcomes:
-tumor control
-Spinal cord damage

Expected outcomes:
-tumor control
-reduced or absent spinal cord damage

RIBs as online monitoring of vascular damage caused by high doses of radiation



See next talk form Tamara Vitacchio

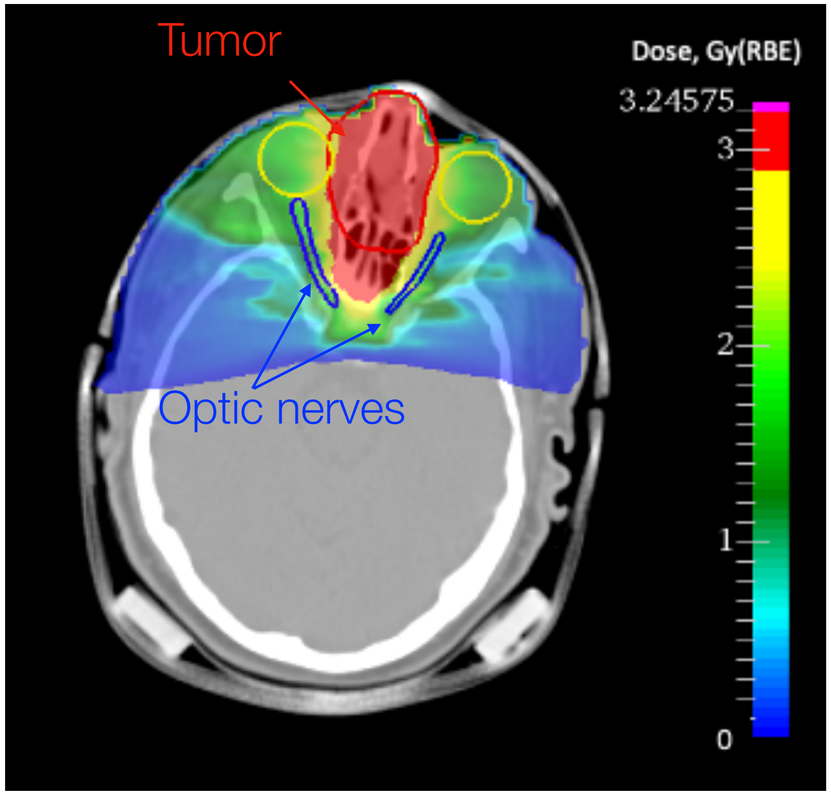
Overview and conclusions

- RIB might be an ideal bullet for image-guided radiotherapy: they are expected to improve the treatment precision and widen the therapeutic window by reducing NTCP
- At GSI-FAIR $^{10,11}C$ and ^{15}O ion beams have been produced with intensities of 10^6 -10^7 particles/s and 99% purity
- RIBs have been characterized in terms of depth-dose profiles, spot size and momentum spread
- The first RIB PET images in plastic phantom were acquired with two different PET setups reaching a spatial resolution < 1 mm
- Commissioning of RIB in the medical cave of GSI. First proof-of-concept animal experiment is planned for 2024 (next talk form Tamara Vitacchio)
- The ambition is to fully exploit the Bragg peak and improve the precision and image-guidance, giving the opportunity to treat new targets in oncology and non-malignant diseases.

Acknowledgments

...and many others!

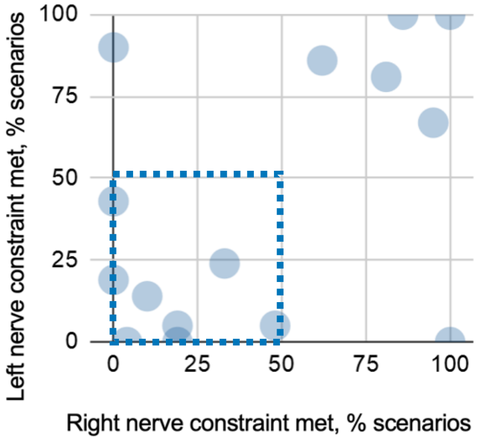
What can we gain? A treatment planning study



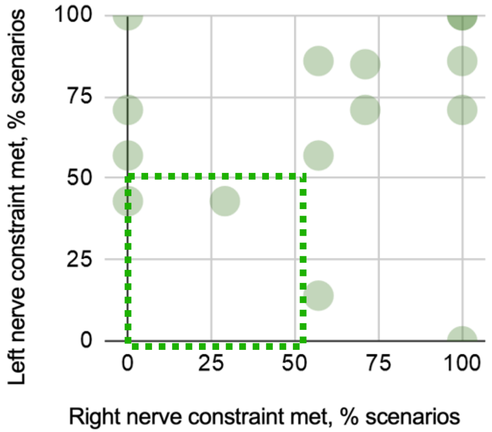
Adenoid cystic carcinoma
OAR: optic nerve (serial organ)
15 Patients

Treatment planning outcomes

^{12}C, 3.5% range margin



^{11}C, no range margin

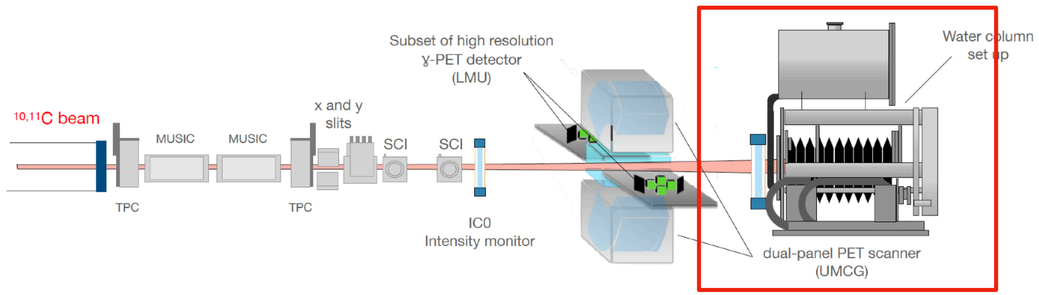


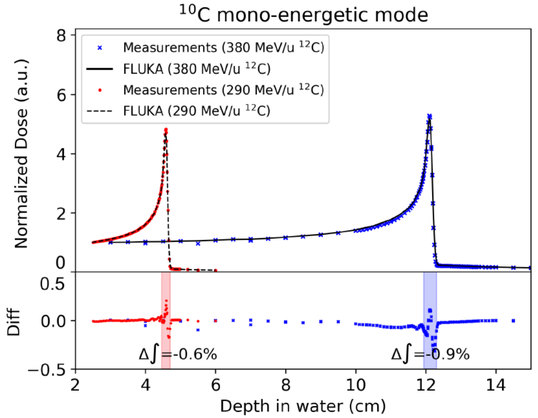
O.Sokol et al. Sci Rep 2022

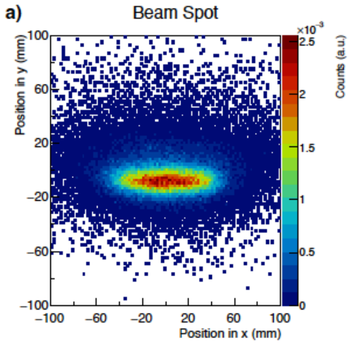
Depth dose profiles measurements

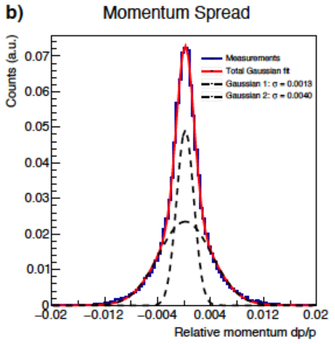
Bragg Curves and ranges in water have been measured with a water column set up in two ion optical modes.

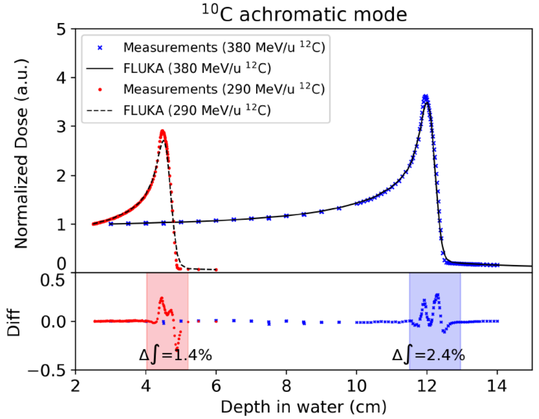
- Depth dose curves to be compared with the measured activity maps.
- Establish the best ion optics to be used for the next BARB experiments

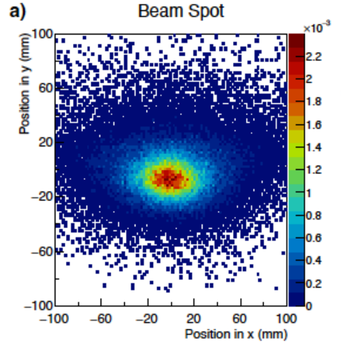


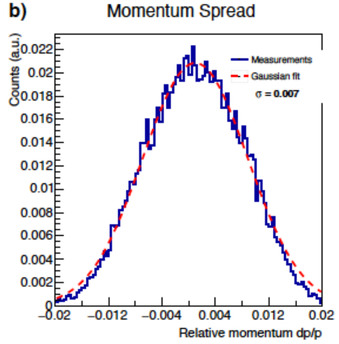












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