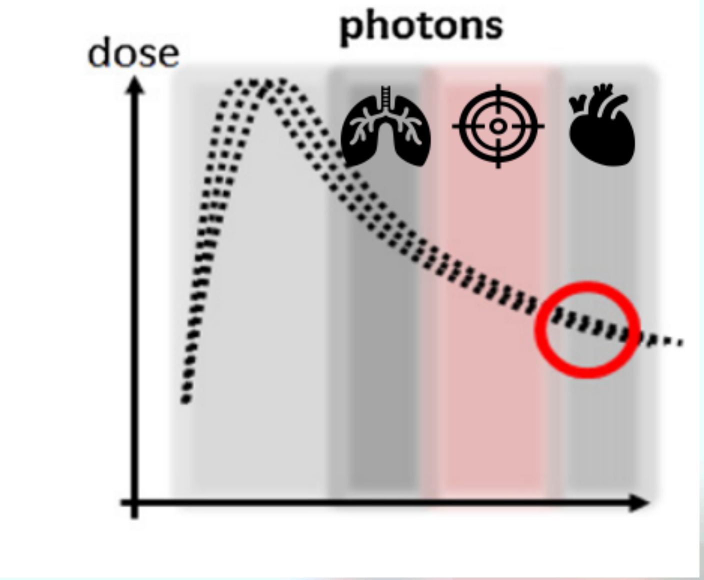
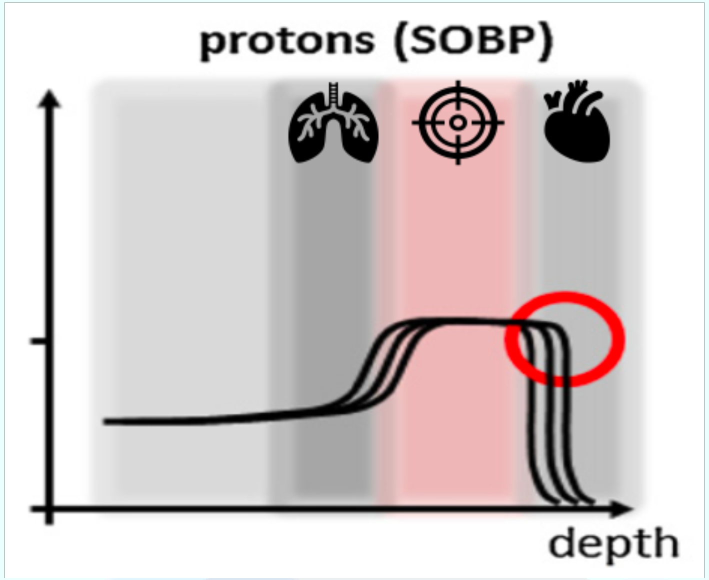
Labeling The Tumor With 31-P, 63-Cu And 89-Y Provides An In Vivo Prompt Gamma-Based Range Verification For Therapeutic Protons

Giorgio Cartechini, *Elena Fogazzi, Luna Pellegri, Marie Vanstalle, S. D. Hart, Chiara La Tessa*

6th July 2023

PROTON RANGE UNCERTAINTIES





Knopf and Lomax 2013 Phys. Med. Biol.

SOURCES OF RANGE UNCERTAINTIES

Systematic:

- CT calibration and resolution
- Mean excitation energy in tissues
- Dose calculation in heterogeneities
- Relative Biological Effectiveness
- …

Random:

- Patient setup
- Beam reproducibility
- Measurements uncertainty in water for commissioning
- …

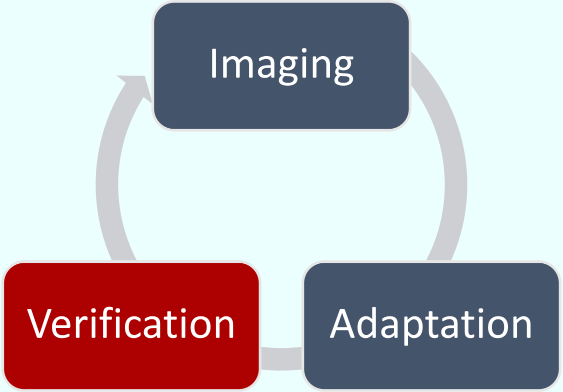
Total uncertainty: 2.4% + 1.2 mm

3-7 mm of uncertainty

Durante and Paganetti Rep. Prog. Phys. (2016)

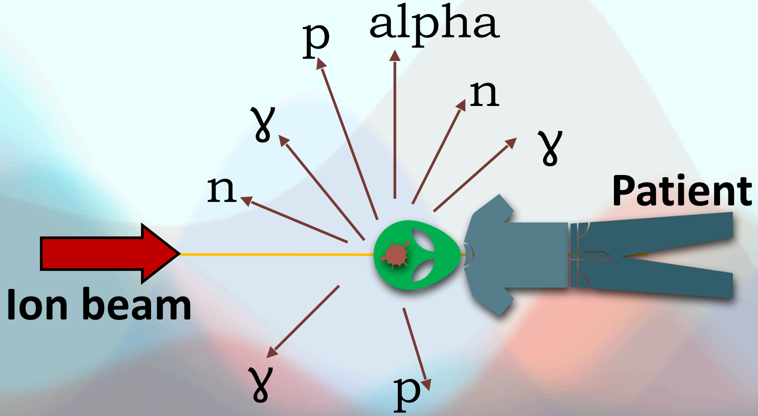
ADAPTIVE RADIO THERAPY

Holy Grail:
Online **detection** and **reaction** to proton range deviations

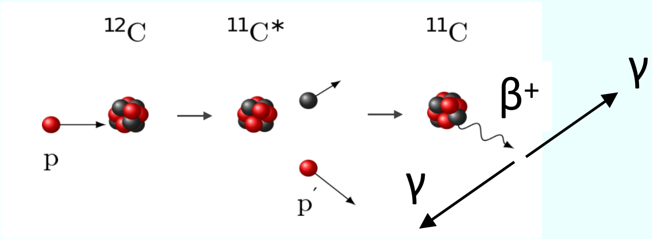


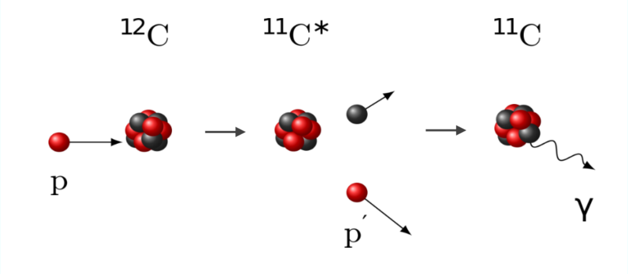
Realistic achievement:
in vivo range verification

- Detect range deviations
- Independent quality assurance



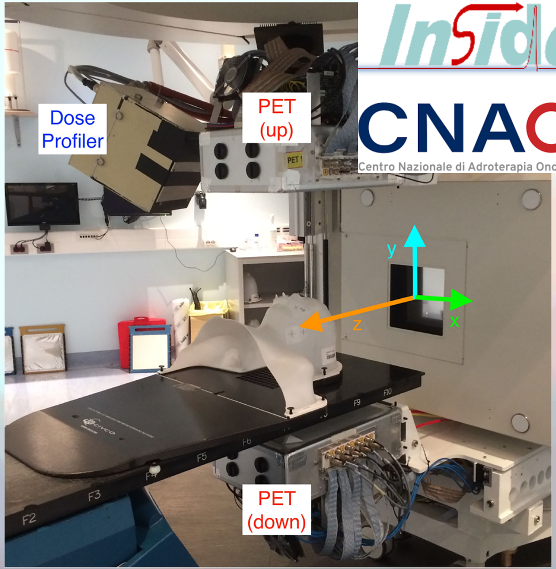
RANGE VERIFICATION TECHNIQUES

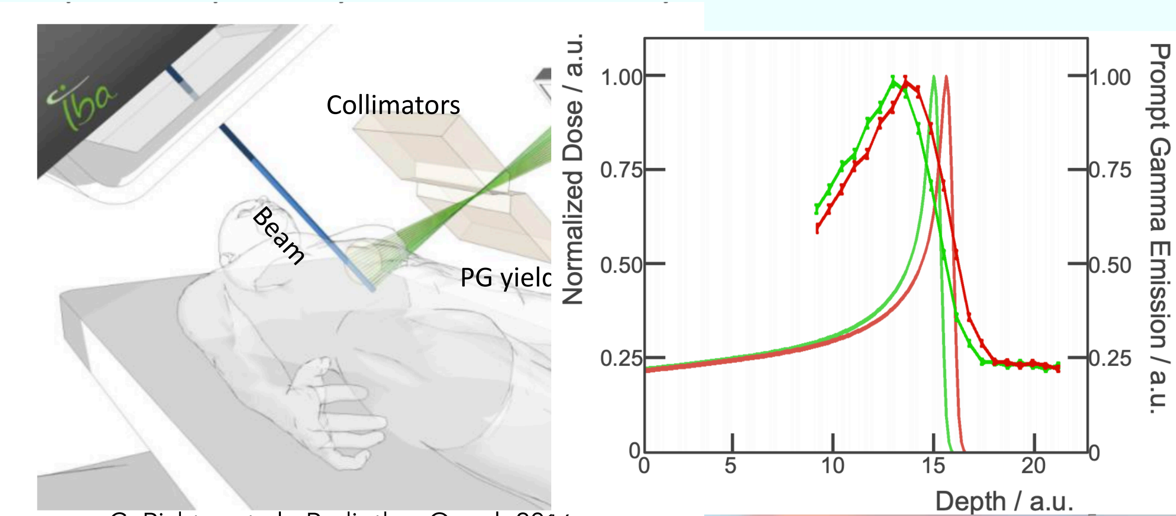




Positron Emission Tomography

Prompt gamma Imaging



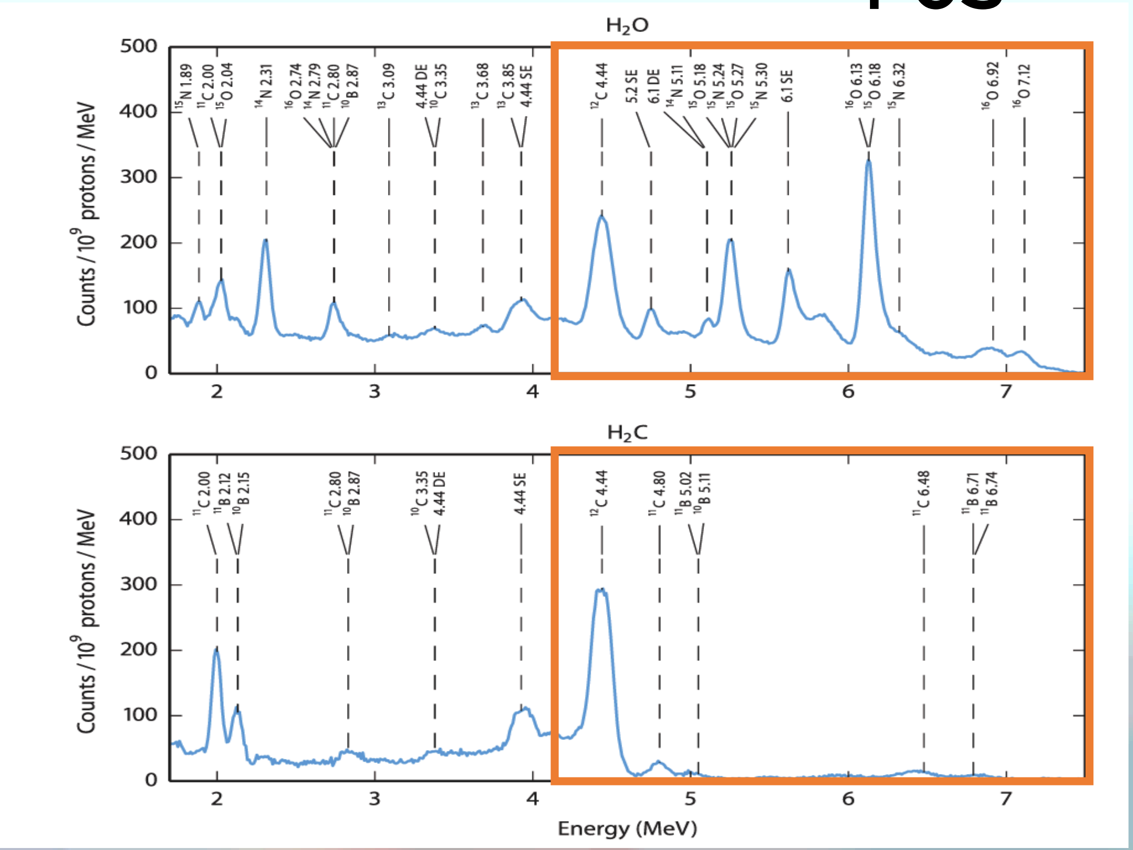


C. Richter et al., Radiother Oncol. 2016

PROMPT GAMMA SPECTROSCOPY-PGS

UNIVERSITY OF TRENTO

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM



PGS can predict **at the same time:**

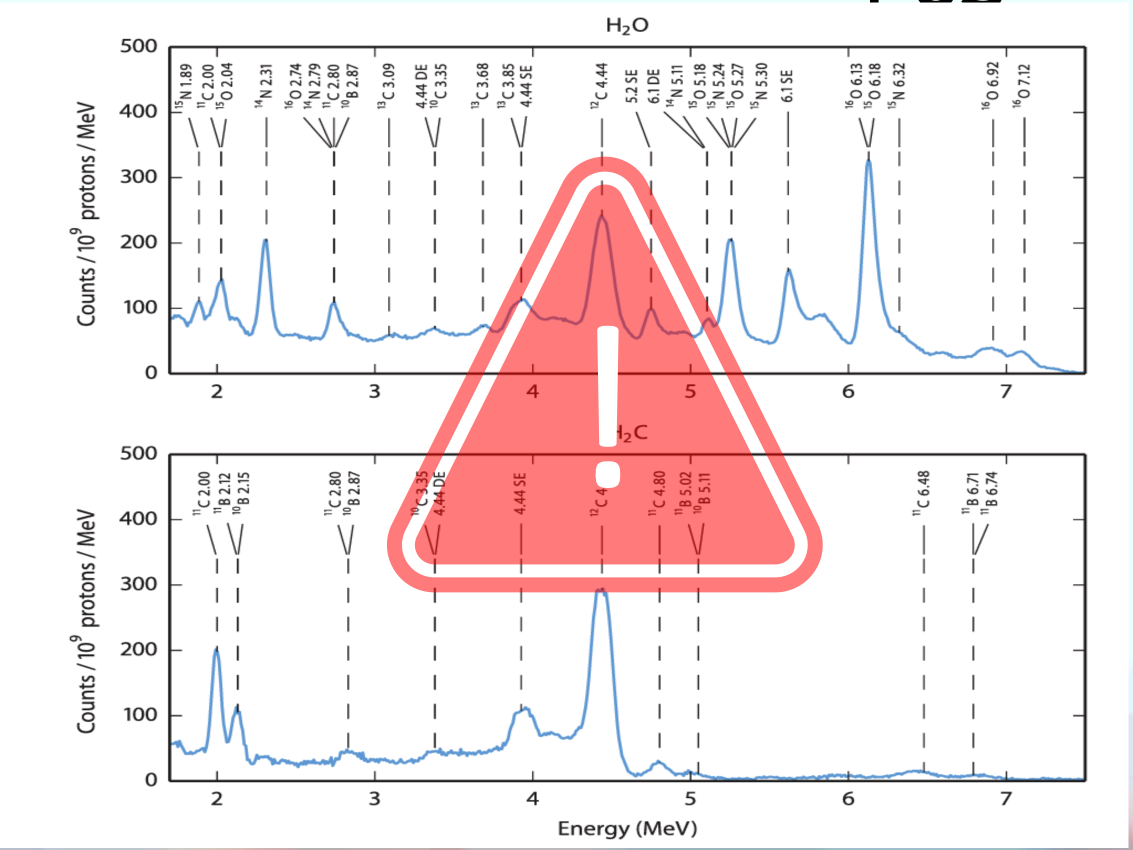
- Absolute proton range
- Elemental material composition

J M Verburg and J Seco, Phys. Med. Biol. 2014 — F Hueso-González et al Phys. Med. Biol. 2018

UNIVERSITY OF TRENTO

PROMPT GAMMA SPECTROSCOPY-PGS

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM



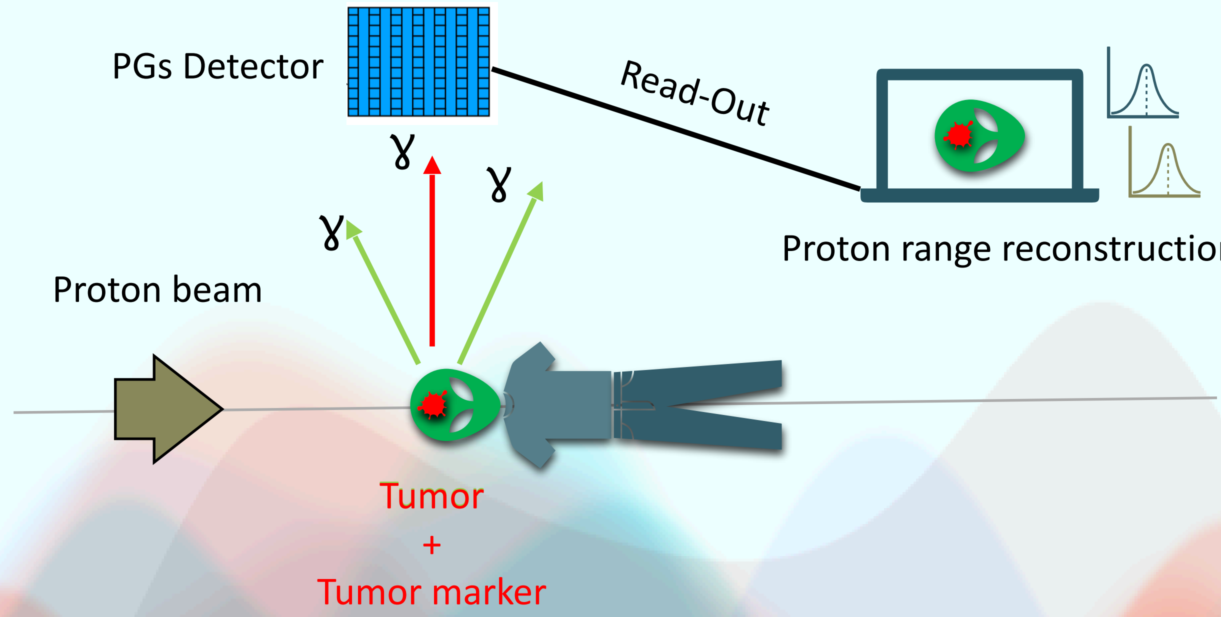
Main limitation: PG statistics

10^7-10^8 protons per Bragg curve result in 2-3 mm range accuracy

J M Verburg and J Seco, Phys. Med. Biol. 59 (2014) 7089

A DIFFERENT APPROACH

What if the tumor could be loaded with a “marker element” that can not only enhance the production of PG but also emit a signature spectrum?



Similar approach already proposed using metal nanoparticles or inserts

Penninckx, Sébastien, et al. Radiation 1.4 (2021): 305-316

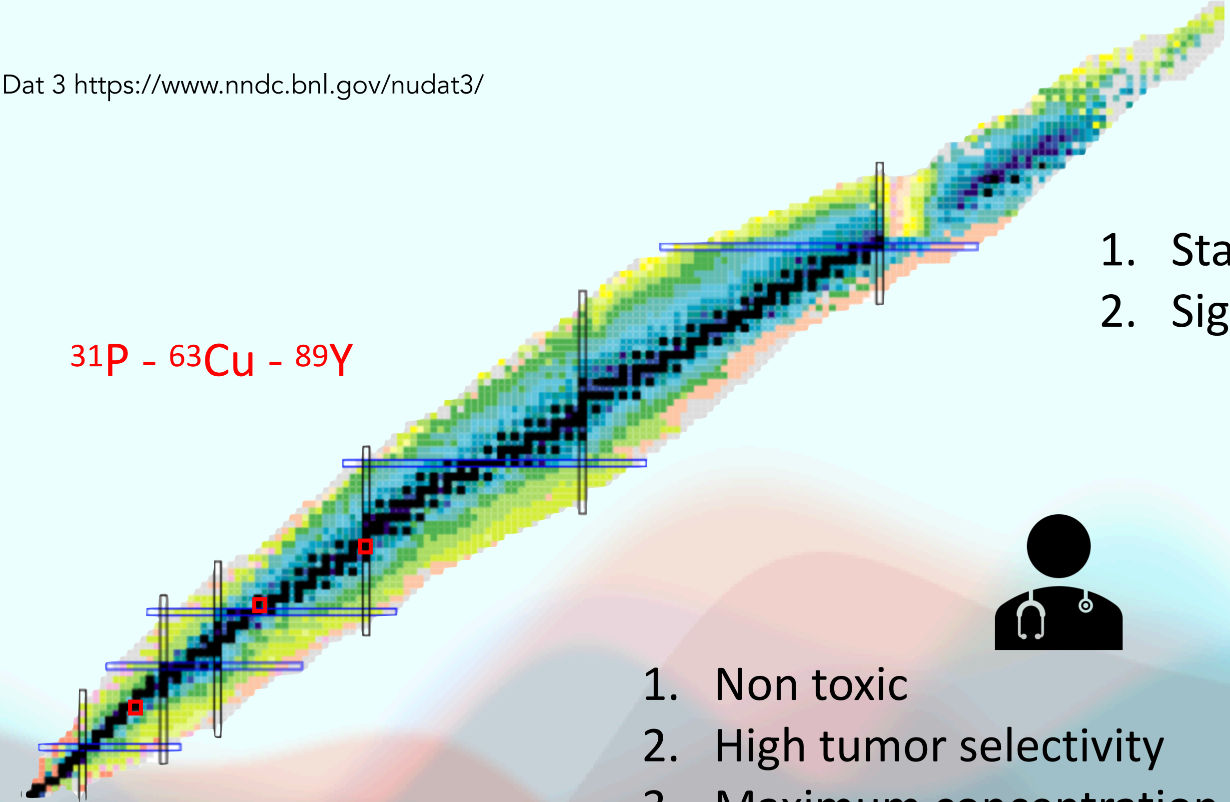
UNIVERSITY OF TRENTO

MARKER ELEMENT

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

NuDat 3 https://www.nndc.bnl.gov/nudat3/

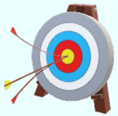
^{31}P - ^{63}Cu - ^{89}Y



1. Stable
2. Signature PG spectrum

1. Non toxic
2. High tumor selectivity
3. Maximum concentration achievable

EXPERIMENTAL MEASUREMENTS

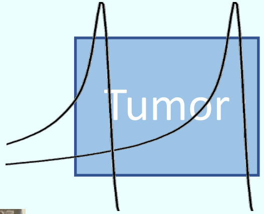


- PG spectroscopy measurements
- Characterization of PG emission spectra from ^{31}P, ^{63}Cu, ^{89}Y targets

Trento proton therapy center, Italy

70 MeV proton beam

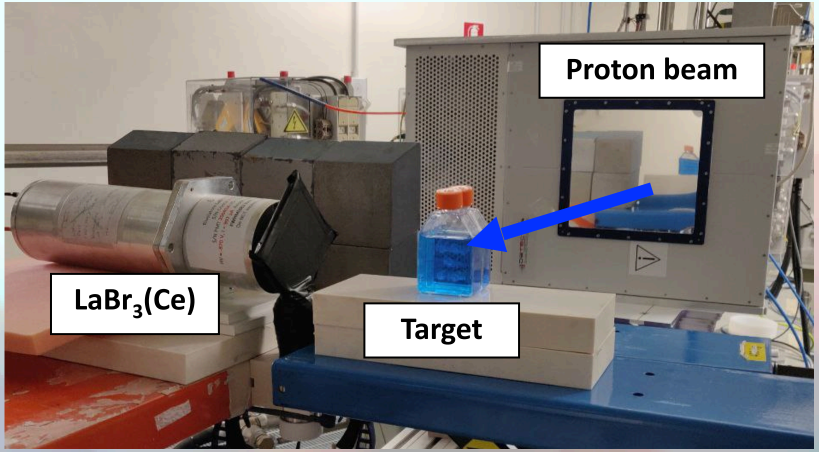
4 cm range in water

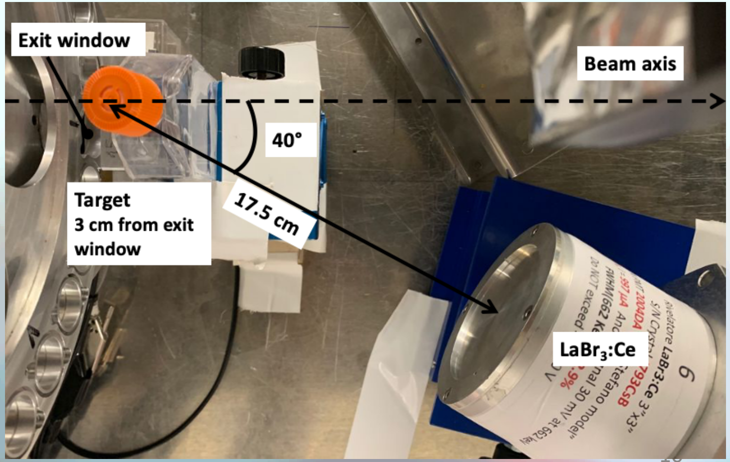


Cyrcè cyclotron Strasbourg, France

25 MeV proton beam

0.5 cm range in water

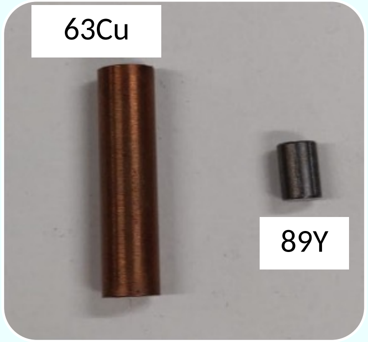




TARGETS

Solid targets

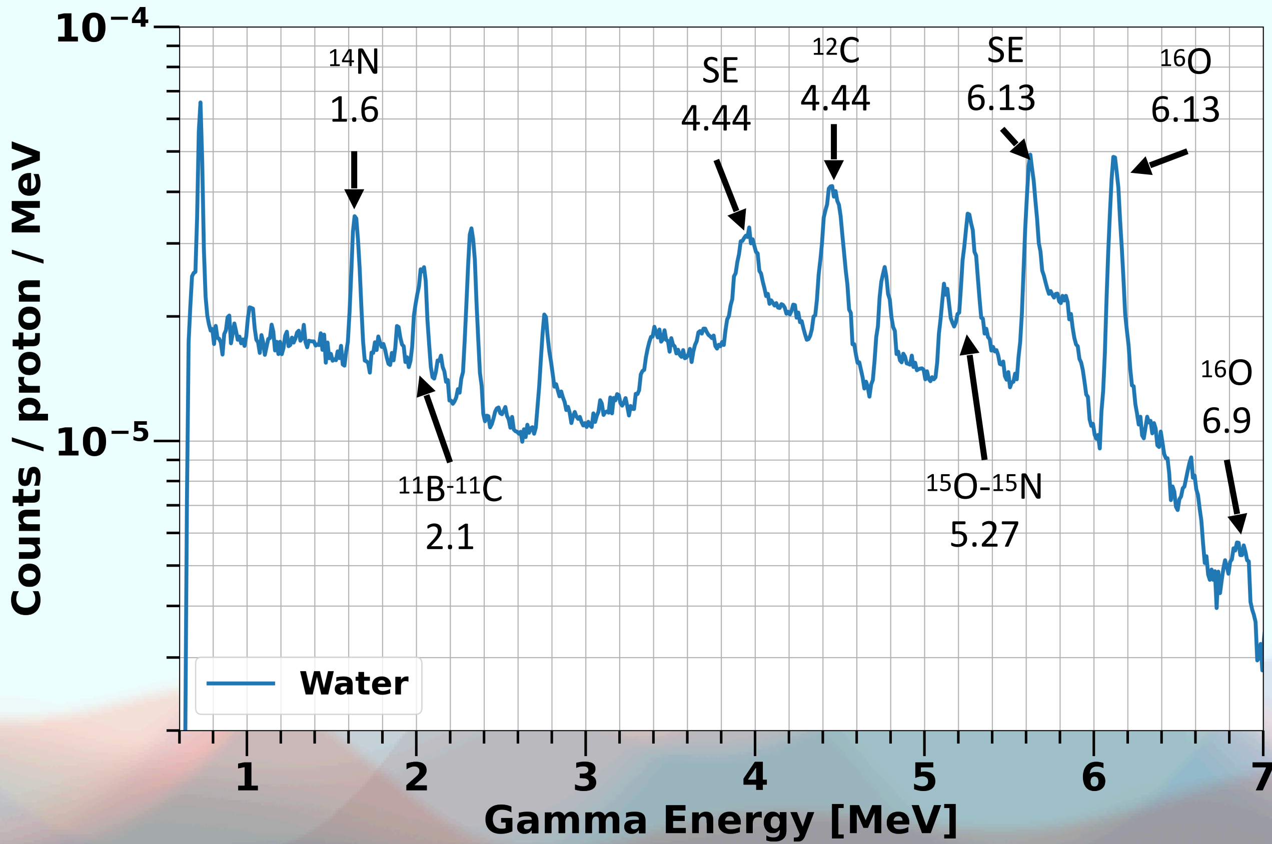
- 100% element concentration
- Only 63Cu and 89Y



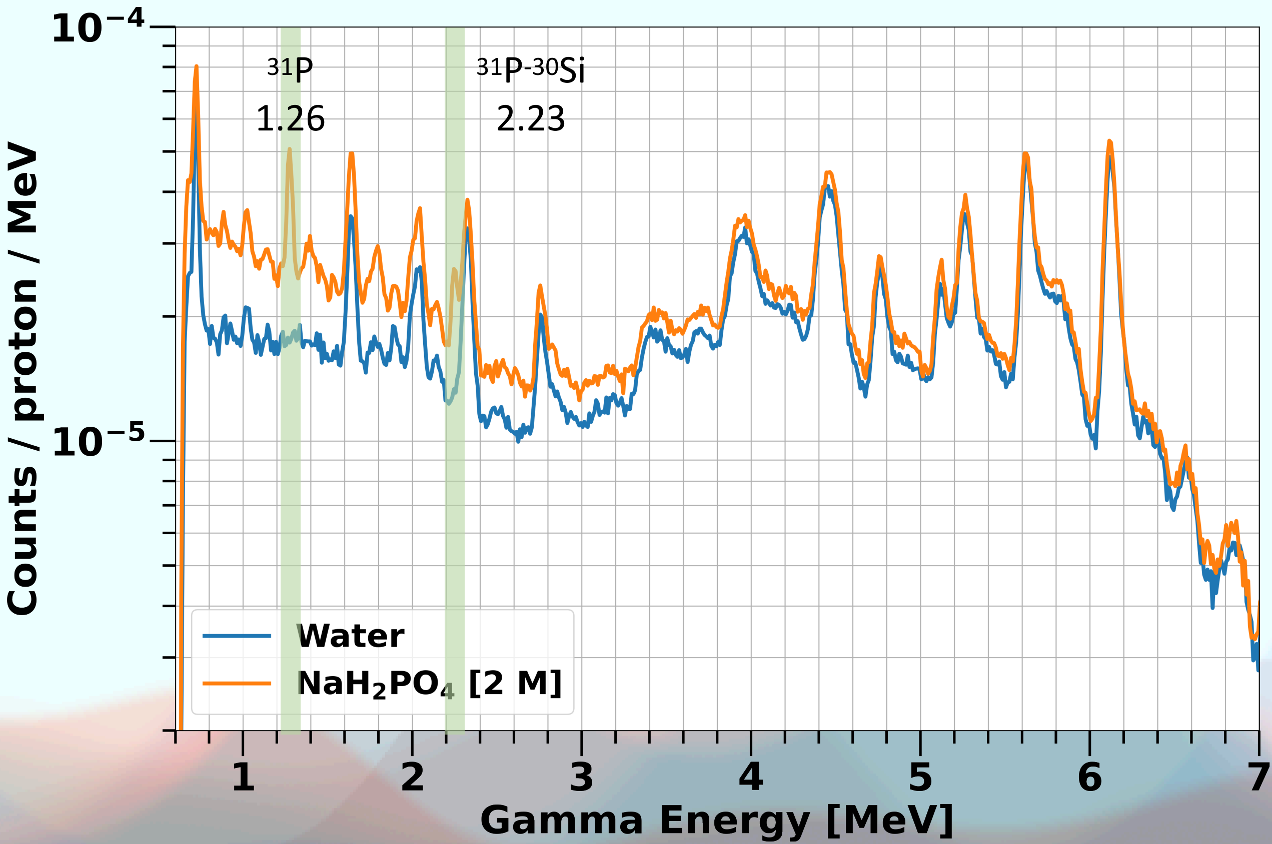
Water-based solutions:

- $NaH_2PO_4 + H_2O$
- $CuSO_4 + H_2O$
- $Y(NO_3)_3 + H_2O$
- Pure water
- 5% to 0.1% mass fraction

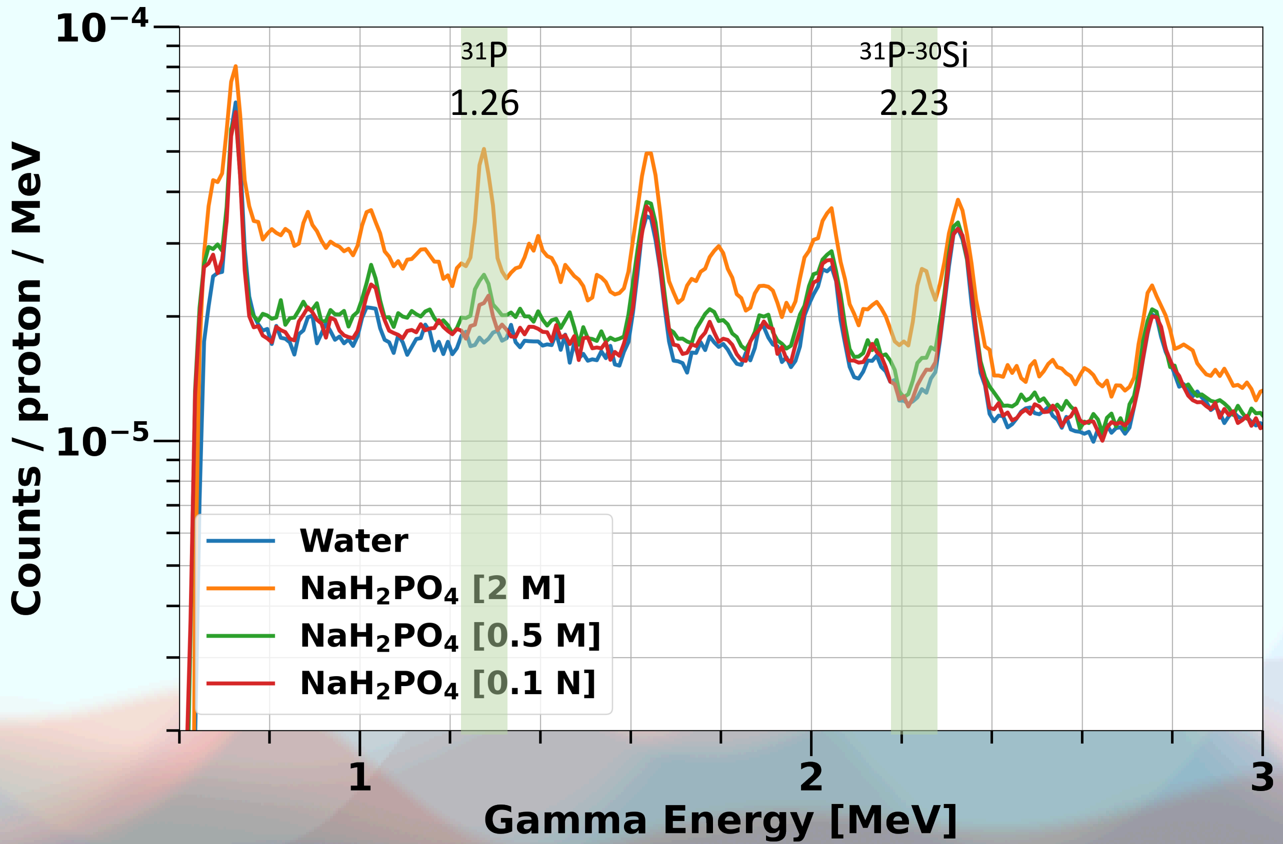
PG ENERGY SPECTRUM: 70 MeV + H_2O



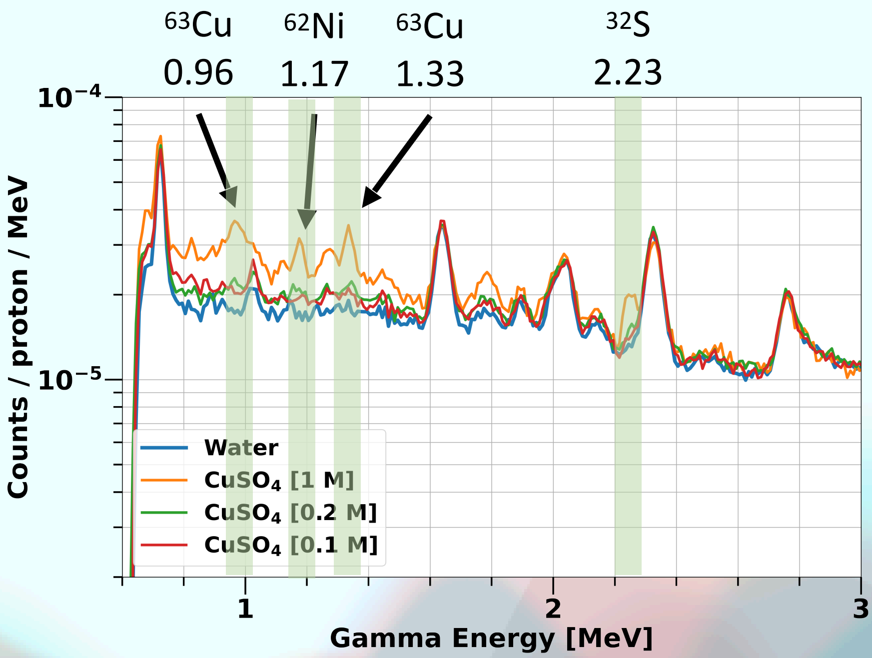
PG ENERGY SPECTRUM: 70 MeV + NaH_2PO_4

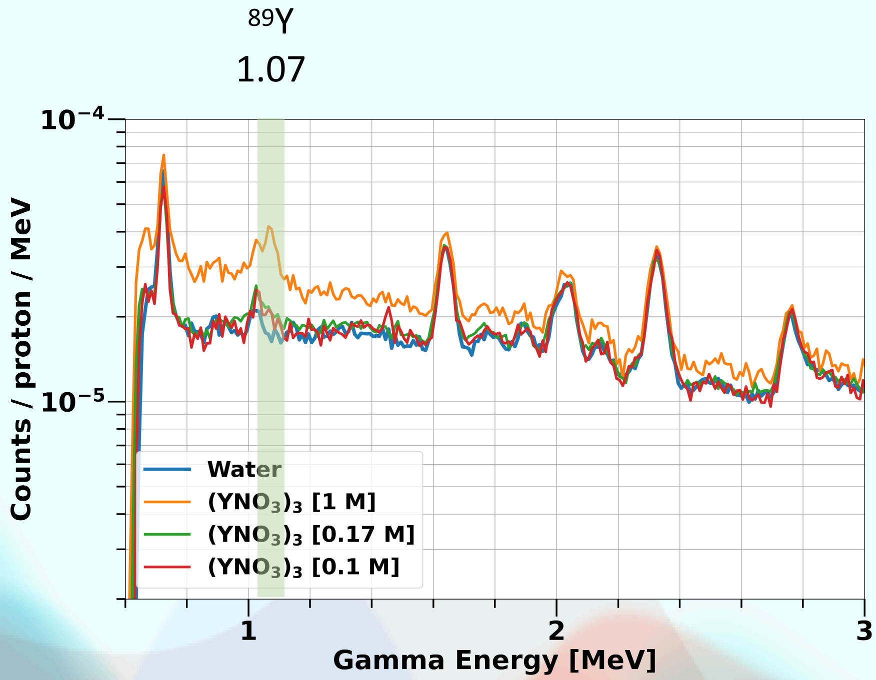


PG ENERGY SPECTRUM: 70 MeV + NaH_2PO_4

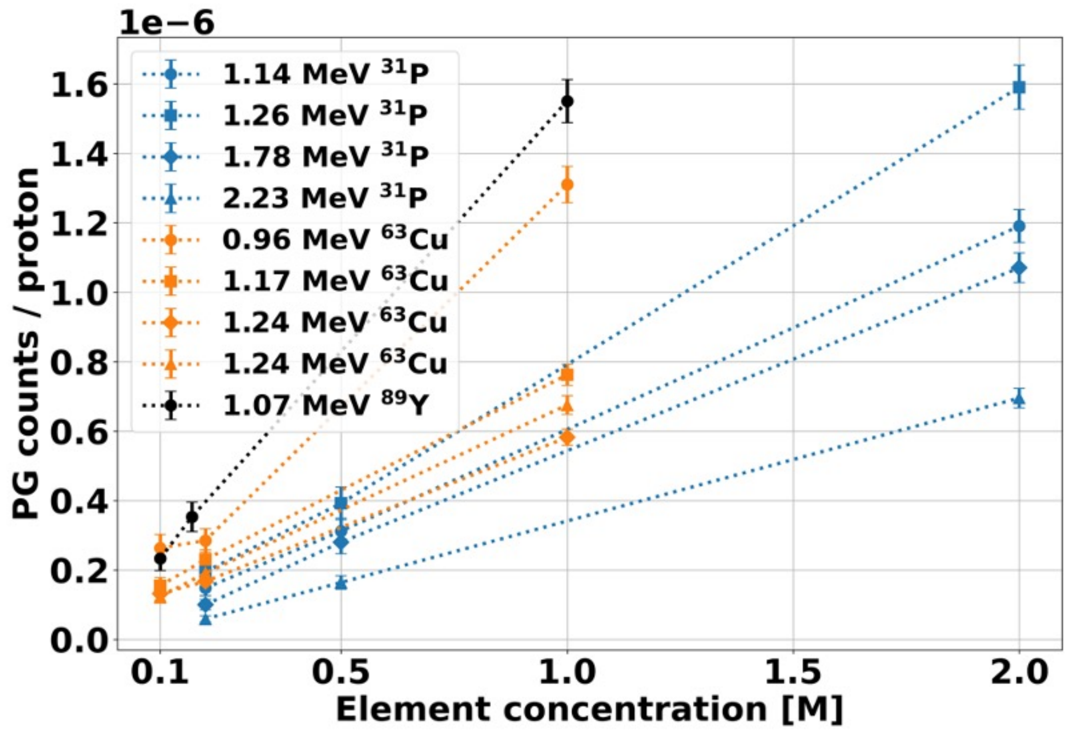


PG ENERGY SPECTRUM: 70 MeV + $CuSO_4$ and $Y(NO_3)_3$





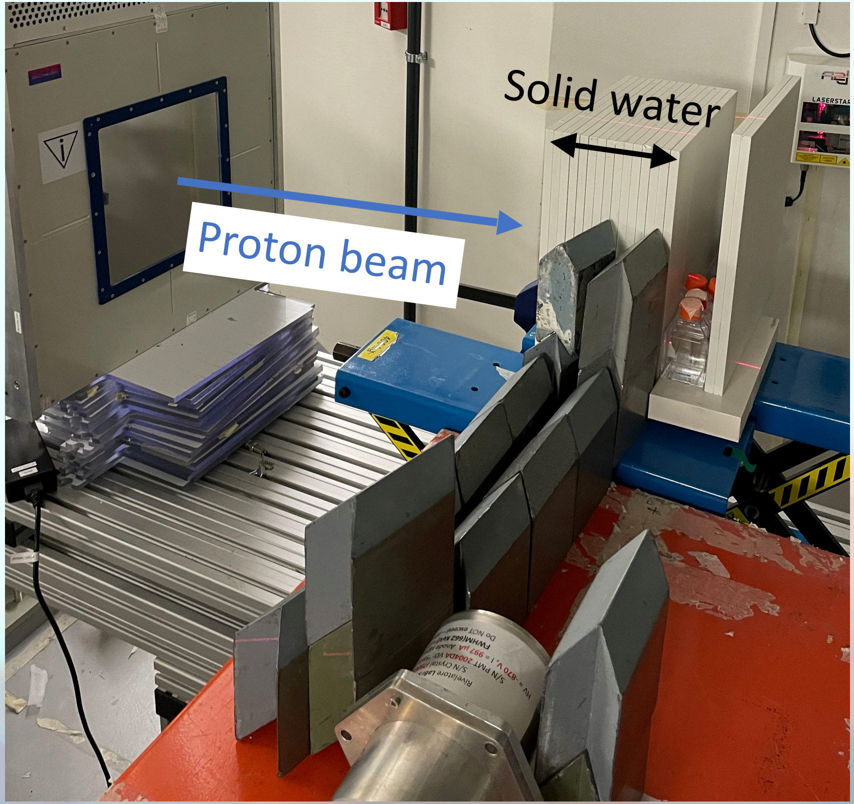
EXTRAPOLATION AT REALISTIC CONCENTRATIONS

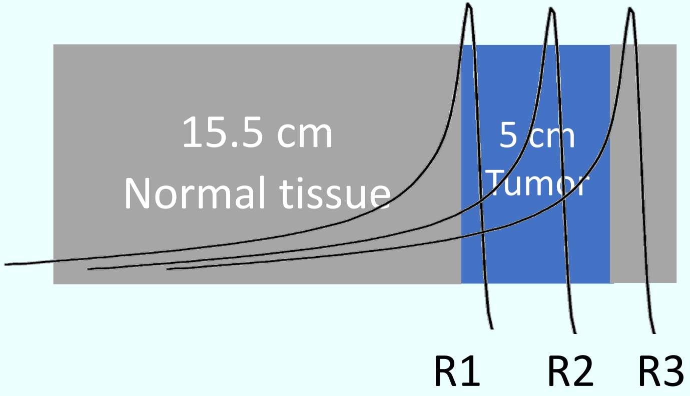


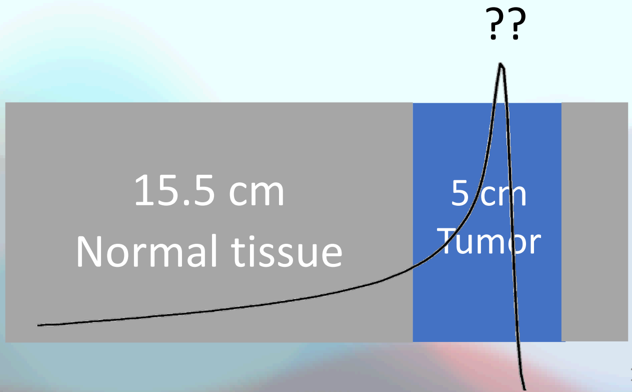
- Assumptions:
  - **0.4 mM** element concentration in tumor
  - **10^9** delivered protons
  - **5 sr** detector solid angle

Element	PG counts above background
^{31}P	34 (5)
^{63}Cu	45 (7)
^{89}Y	22 (5)

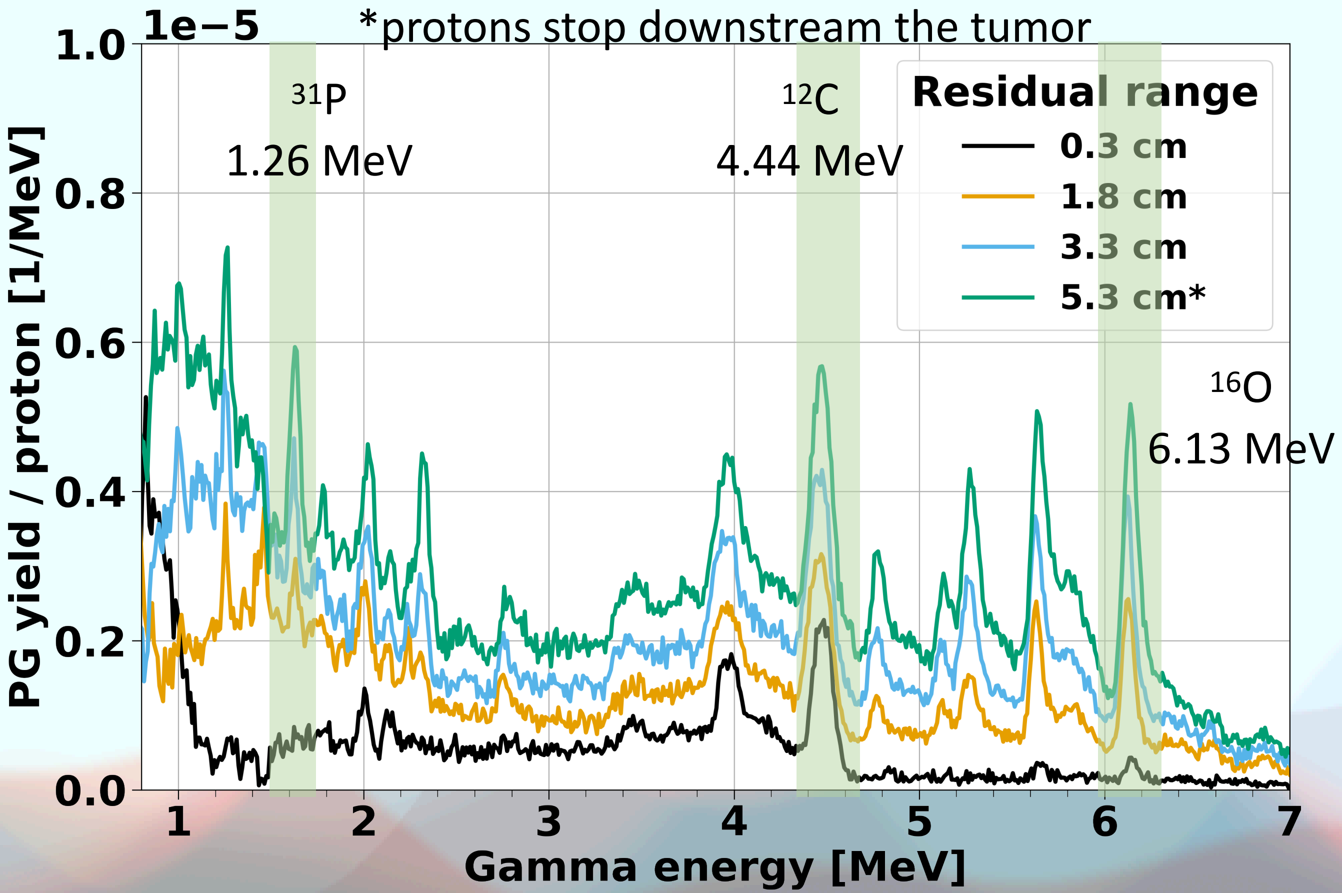
PROTON RANGE APPLICATION: SIMPLE GEOMETRY



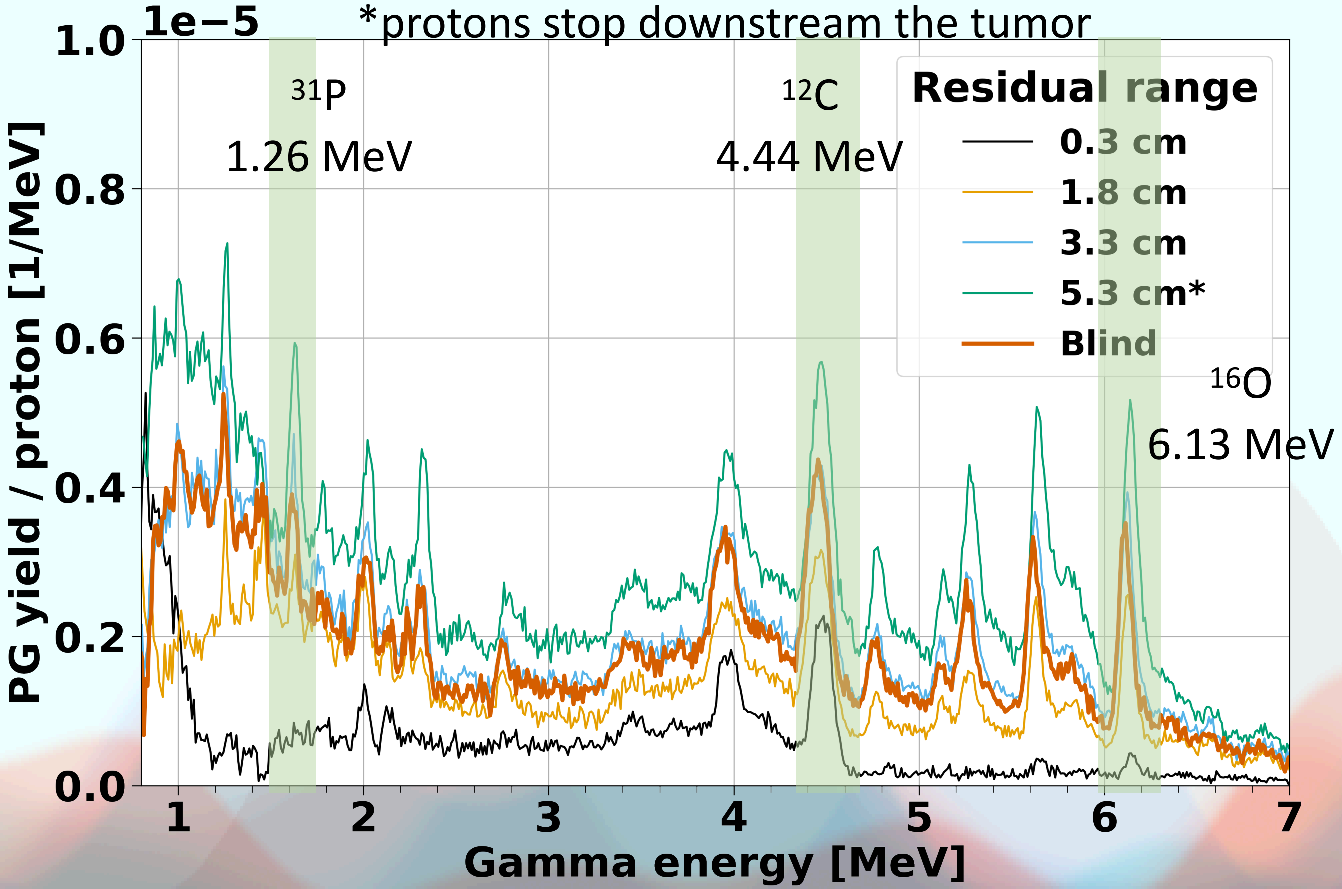


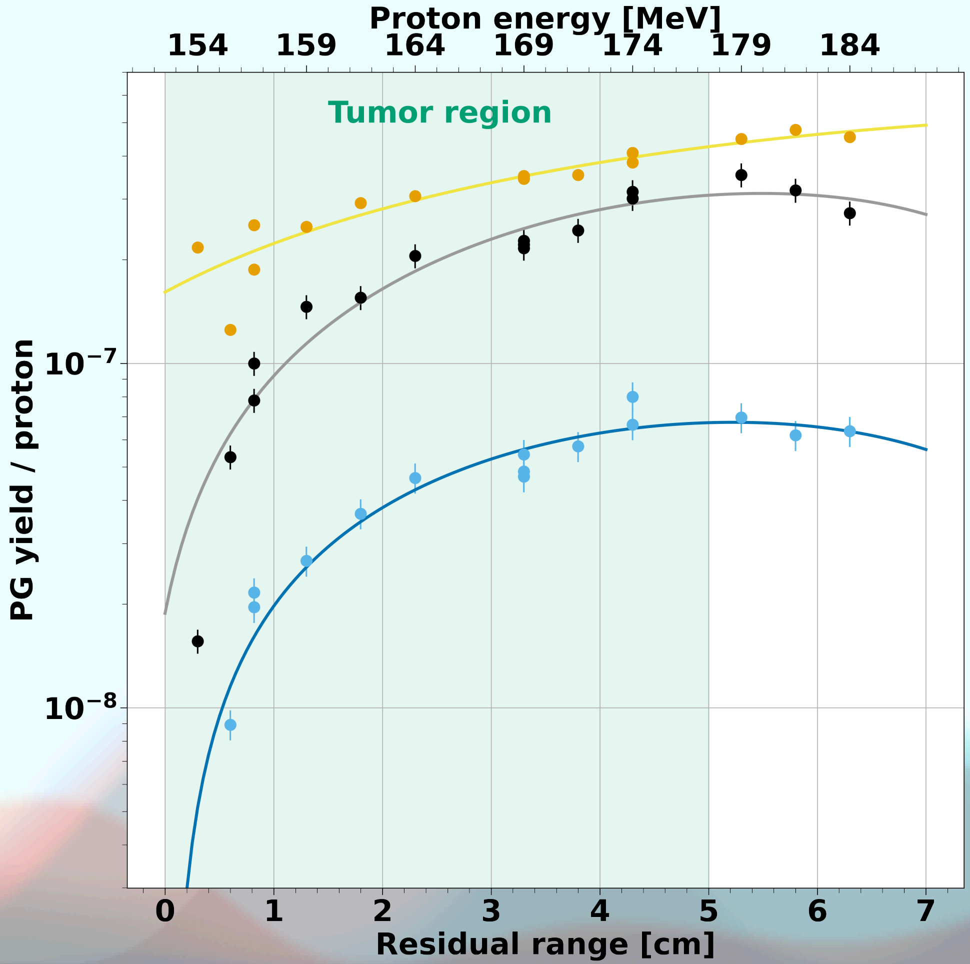


SIMPLIFIED SETUP



SIMPLIFIED SETUP



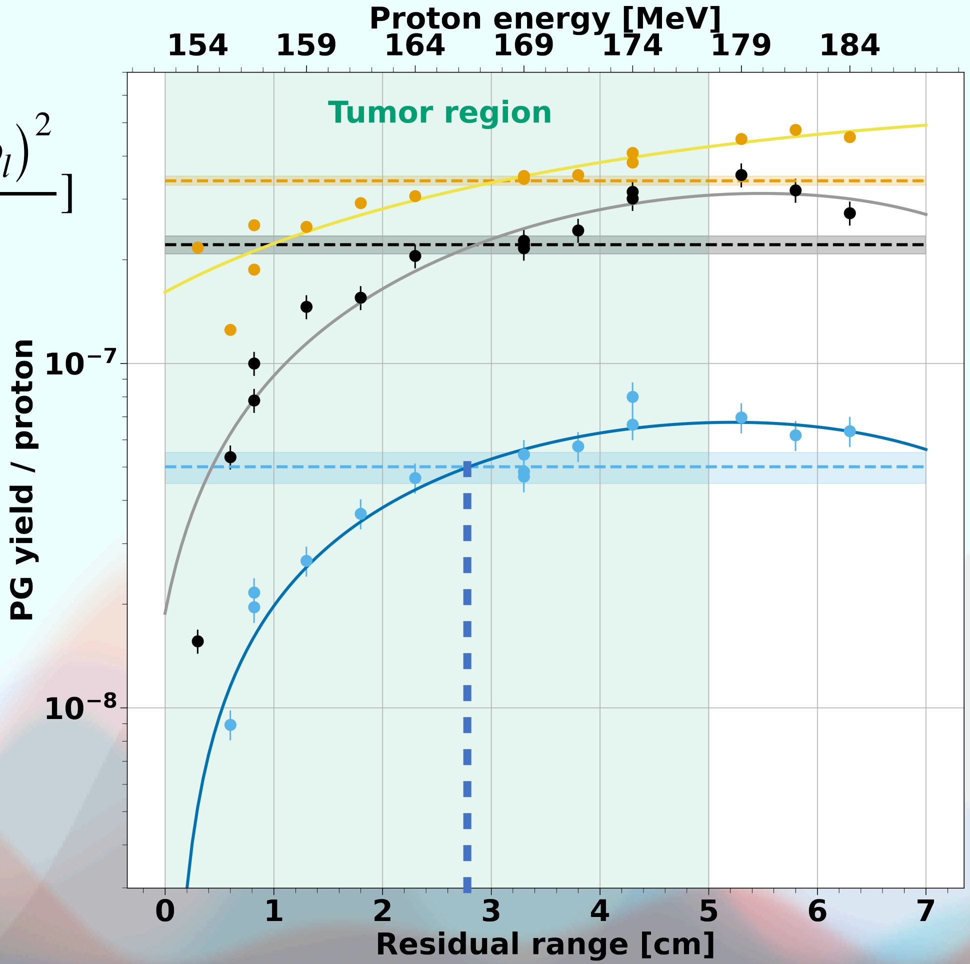


4.44 MeV ^{12}C

6.13 MeV ^{16}O

1.26 MeV ^{31}P

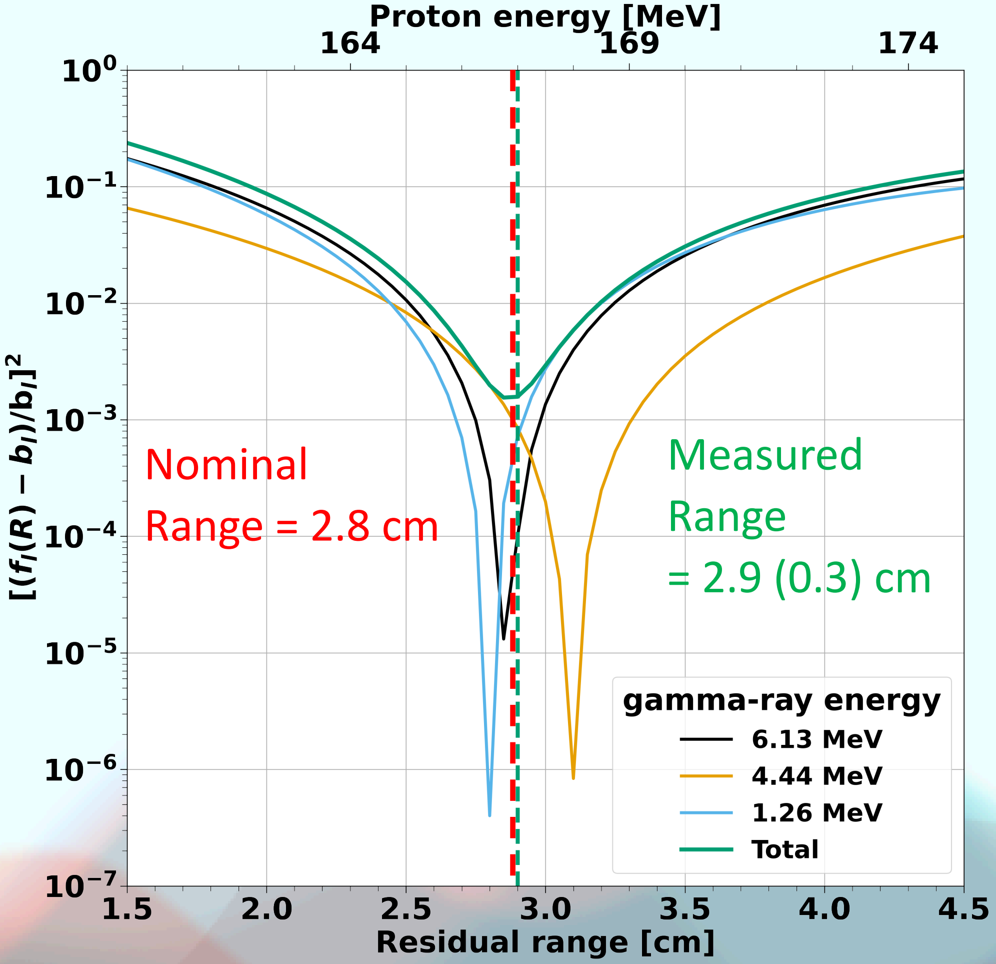
$$\min\left[\sum_l \frac{\left(f_l(R) - b_l\right)^2}{b_l^2}\right]$$



4.44 MeV ^{12}C

6.13 MeV ^{16}O

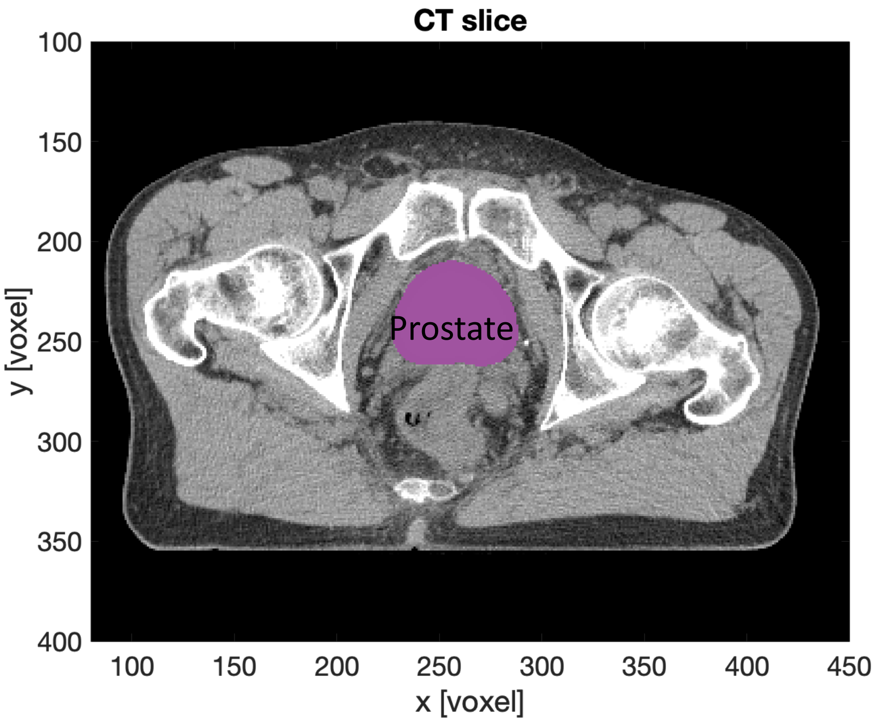
1.26 MeV ^{31}P



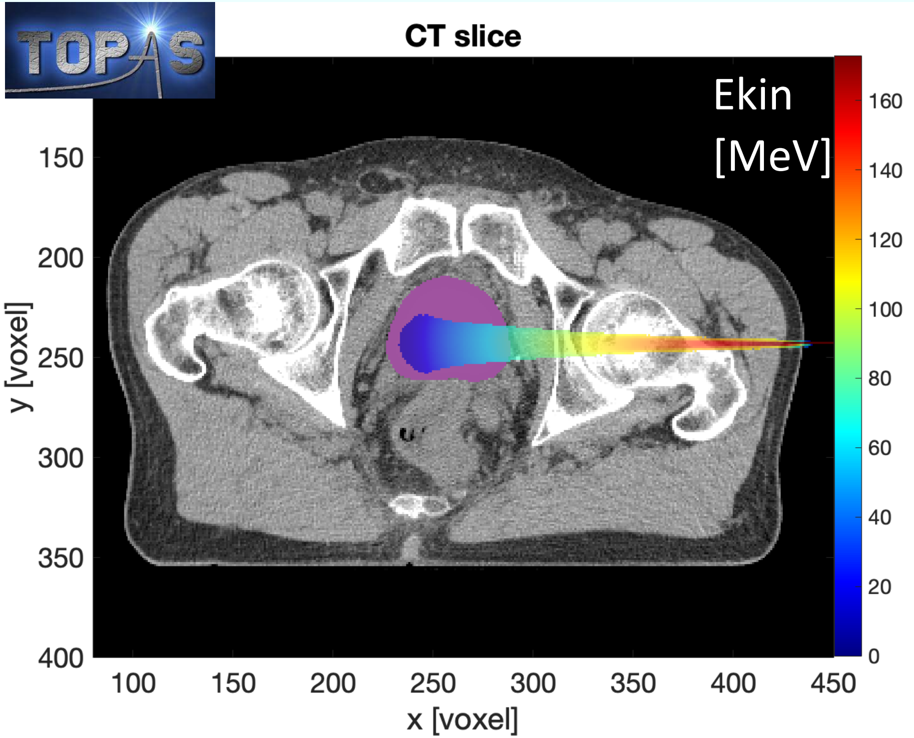
$$\min\left[\sum_l \frac{\left(f_l(R) - b_l\right)^2}{b_l^2}\right]$$

NEXT STEP: REAL PATIENT GEOMETRY

1. Label the target with 31P, 63Cu, 89Y



2. Simulation of proton interaction in patient

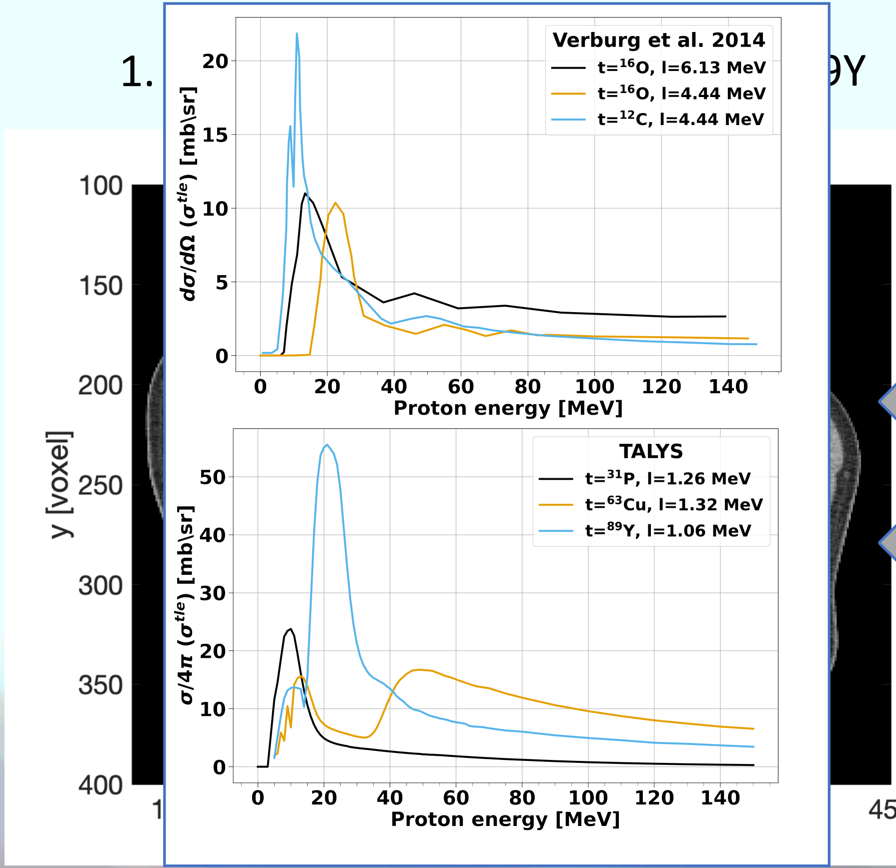


UNIVERSITY OF TRENTO

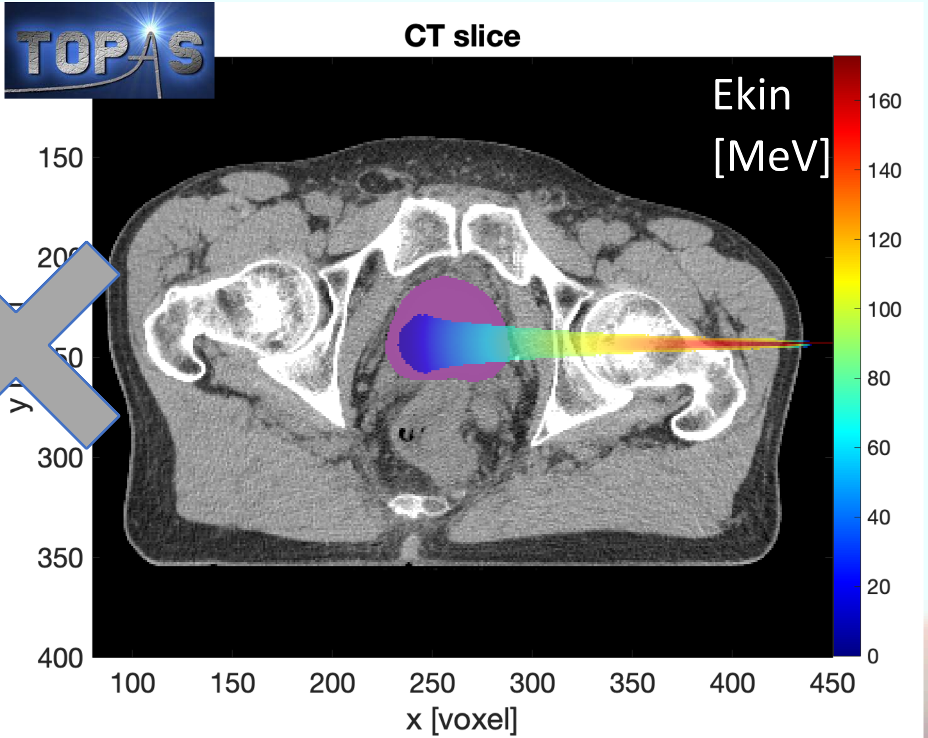
SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

NEXT STEP: REAL PATIENT GEOMETRY

1. … 9Y



2. Simulation of proton interaction in patient



TAKE HOME MESSAGE

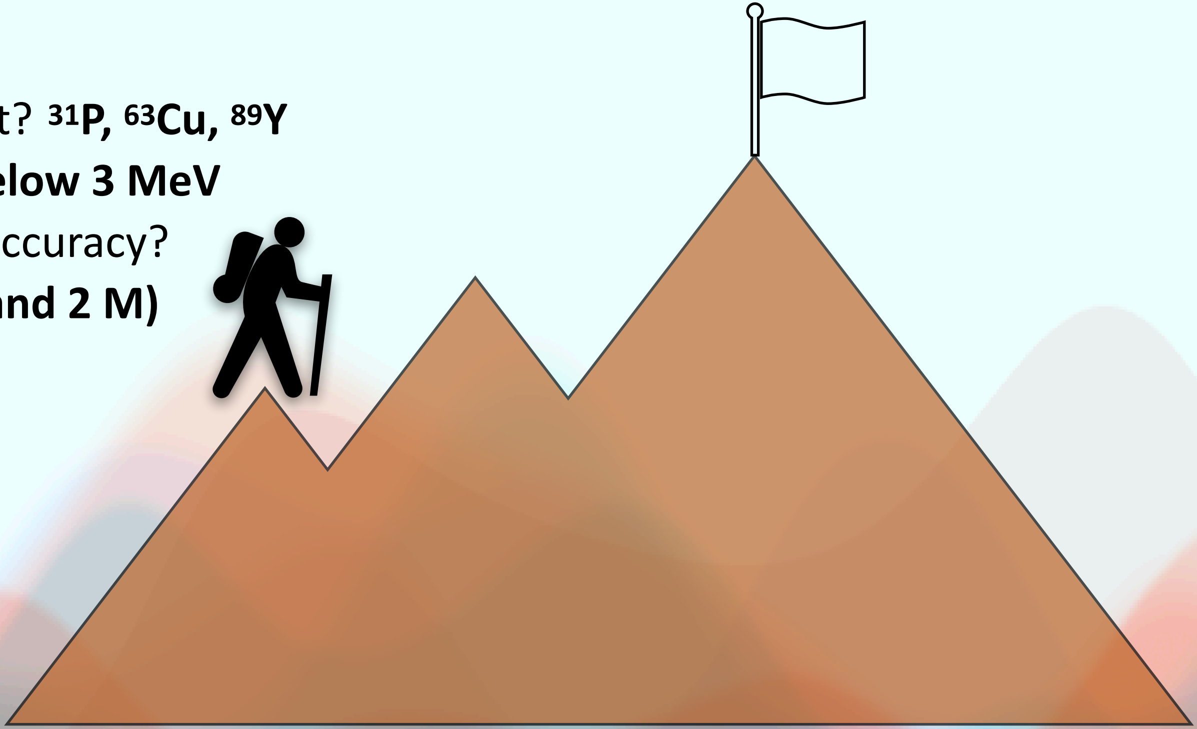
UNIVERSITY OF TRENTO

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

To investigate the feasibility of a novel in vivo range verification approach

Physics

- Which element? **^{31}P, ^{63}Cu, ^{89}Y**
- Which PGs? **Below 3 MeV**
- Proton range accuracy? **3 mm (10^{11} p and 2 M)**

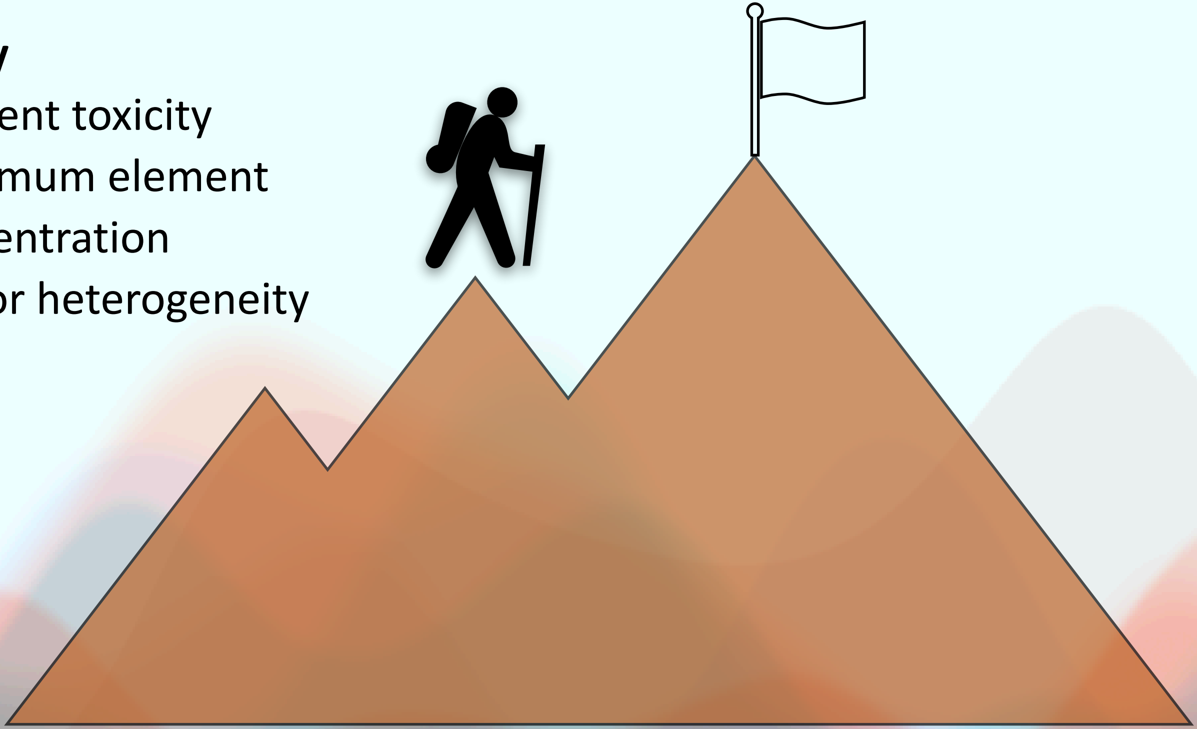


TAKE HOME MESSAGE

To investigate the feasibility of a novel in vivo range verification approach

Biology

- Element toxicity
- Maximum element concentration
- Tumor heterogeneity

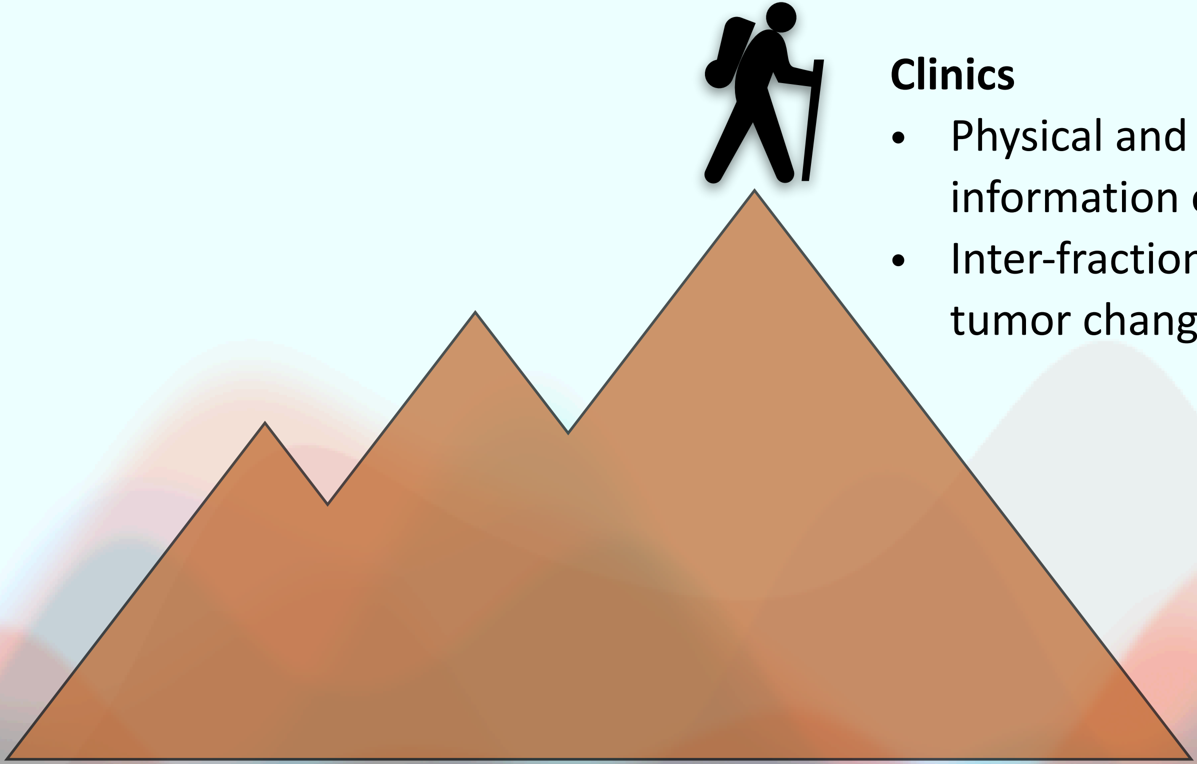


UNIVERSITY OF TRENTO

TAKE HOME MESSAGE

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

To investigate the feasibility of a novel in vivo range verification approach



Clinics

- Physical and biological information on the treatment
- Inter-fraction physiological tumor change

UNIVERSITY OF TRENTO

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

THANK YOU

frontiers | Frontiers in Physics

https://doi.org/10.3389/fphy.2023.1071981

Loading the tumor with ^{31}P, ^{63}Cu and ^{89}Y provides an *in vivo* prompt gamma-based range verification for therapeutic protons

Giorgio Cartechini[1,2,3], Elena Fogazzi[1,2], Shanyn-Dee Hart[4,5], Luna Pellegri[4,5], Marie Vanstalle[6], Michela Marafini[7,8] and Chiara La Tessa[1,2,3]*

[1]Department of Physics, University of Trento, Trento, Italy, [2]Trento Institute for Fundamental Physics and Applications, Istituto Nazionale di Fisica Nucleare (TIFPA-INFN), Trento, Italy, [3]Department of Radiation Oncology, University of Miami, Miami, FL, United States, [4]Separated Sector Cyclotron Laboratory, iThemba Laboratory for Accelerator Based Sciences, Somerset West, South Africa, [5]School of Physics, University of the Witwatersrand, Johannesburg, South Africa, [6]Université de Strasbourg, Centre National de la Recherche Scientifique (CNRS), Institut Pluridisciplinaire Hubert Curien (IPHC), Strasbourg, France, [7]Museo Storico della Fisica e Centro Studi e Ricerche Enrico Fermi, Rome, Italy, [8]Istituto Nazionale di Fisica Nucleare (INFN), Section of Roma 1, Rome, Italy