Istituto Nazionale di Fisica Nucleare
SEZIONE DI FIRENZE

A proton Computed Tomography scanner for biological phantoms imaging

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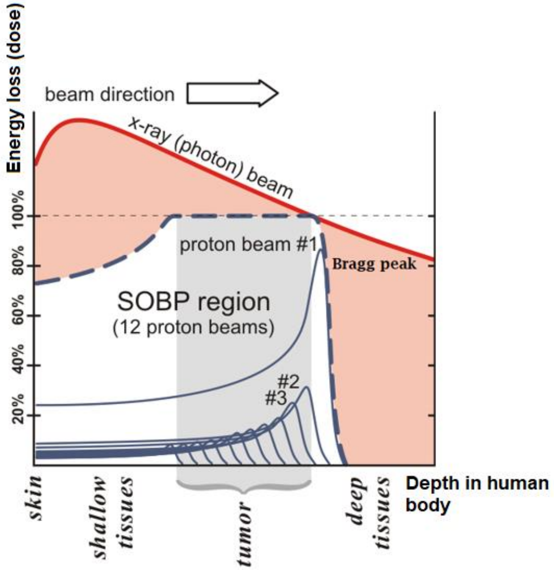
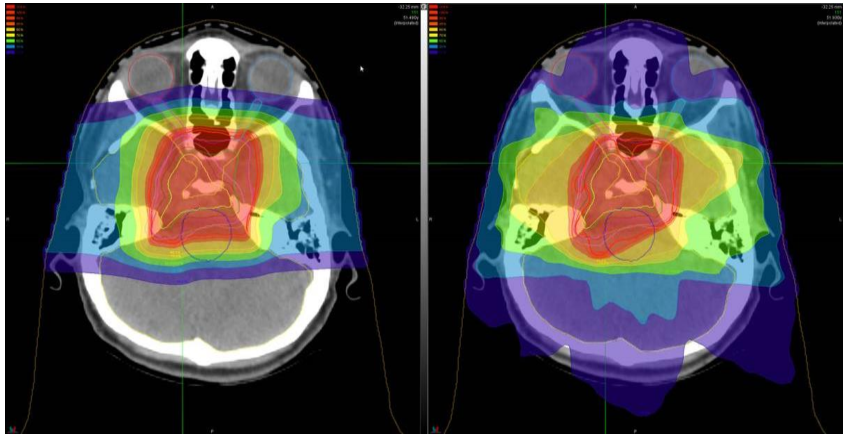
Why proton Computed Tomography?

Hadron therapy exploits the sharp shape of the Bragg peak to precisely irradiate a tumor.



Protons X-rays



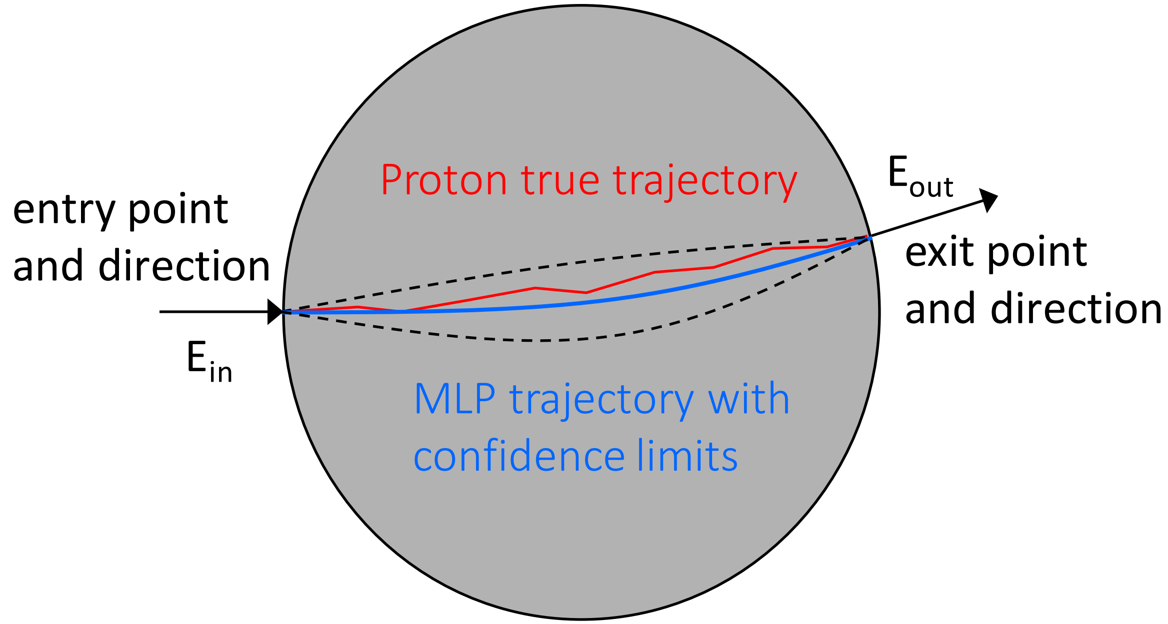
Treatment plans dose comparison

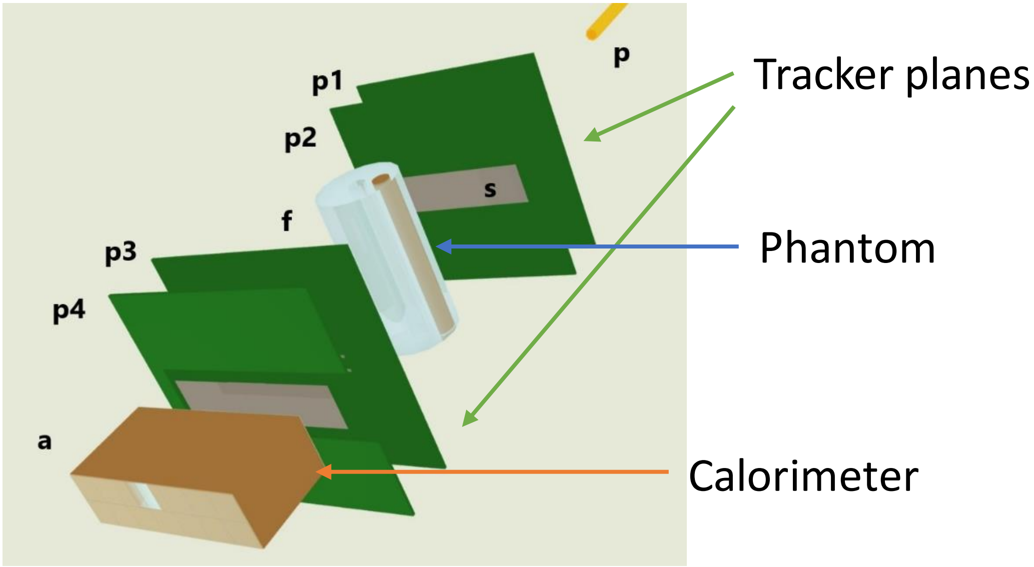
- Treatment planning in hadron therapy requires a precise determination of the proton stopping power distribution (relative to water - **RSP**) within the volume crossed by the beam.
- For this purpose treatment planning systems presently use proton stopping power maps derived from x-ray attenuation coefficients (Hounsfield Units – HU) obtained by a **x-ray CT (xCT)** scan through a calibration procedure.
- This procedure introduces erros → the volume to be irradiated is enlarged by a safety margin which is tipically: +3.5%*range + 1mm

A **proton computed Tomography (pCT)** could **directly measure** the 3D proton relative stopping power maps (RSP) eventually improving treatment planning precision.

How to perform a pCT

- Use a **monoenergetic proton beam** with “known” energy, high enough to cross the phantom to be imaged (~200 MeV)
- In order to deal with Multiple Coulomb scattering: measure **single proton** track and residual energy

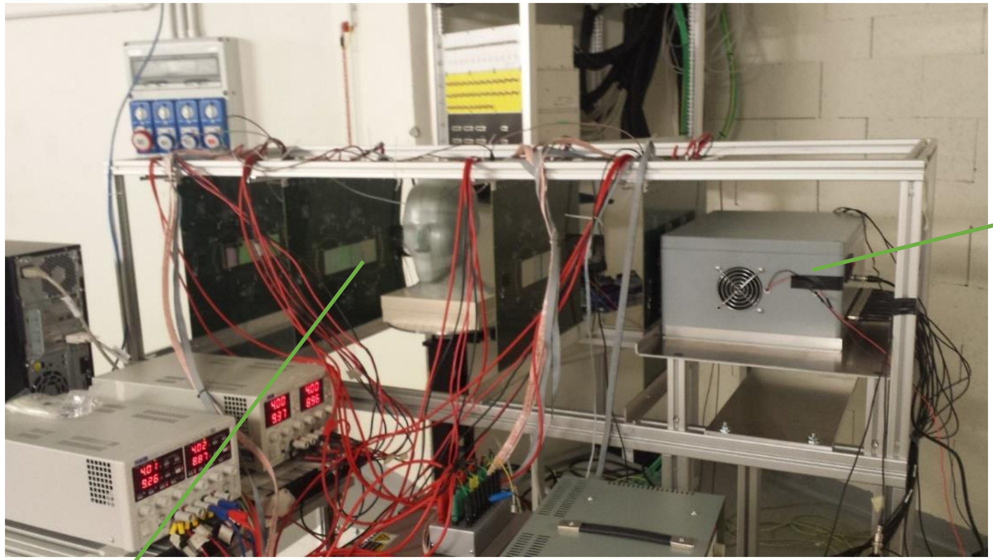




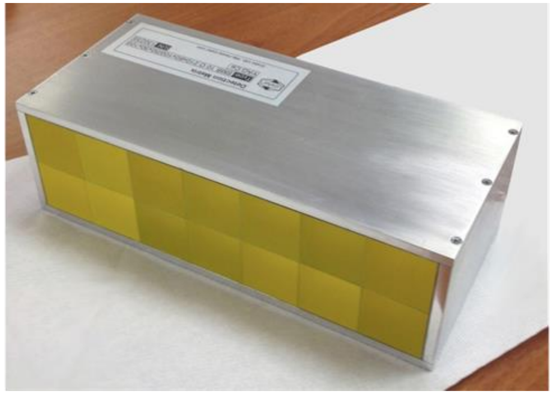
Tracking allows to estimate Most Likely Path [*R.W. Schulte at al. Med. Phys.* ***35 (11)*** *(2008)*]
Residual energy gives information on energy loss inside the phantom
Data are collected from different directions and processed through reconstruction algorithms to compute RSP maps

The INFN pCT apparatus

INFN pCT apparatus mounted at APSS Trento experimental beam line

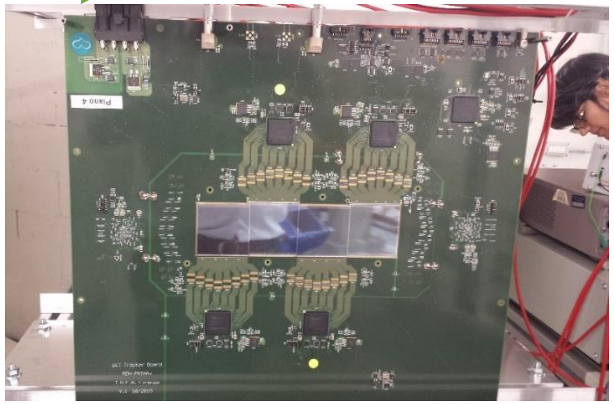


Calorimeter



2x7 YAG:Ce Crystals Array
$3x3x10cm^3$ each
Read-out by Silicon PM

Tracker plane



Tracker composed of 4 xy planes
Each xy plane based on 4x2 silicon microstrip p-on-n detectors, 200μm pitch, 320μm thick, slightly overlapped to ensure hermeticity
$5x20\ cm^2$ active area
80/100 kHz sustained acquisition rate

Carlo Civinini *et al. Phys. Med. Biol. 65 (2020) 225012*

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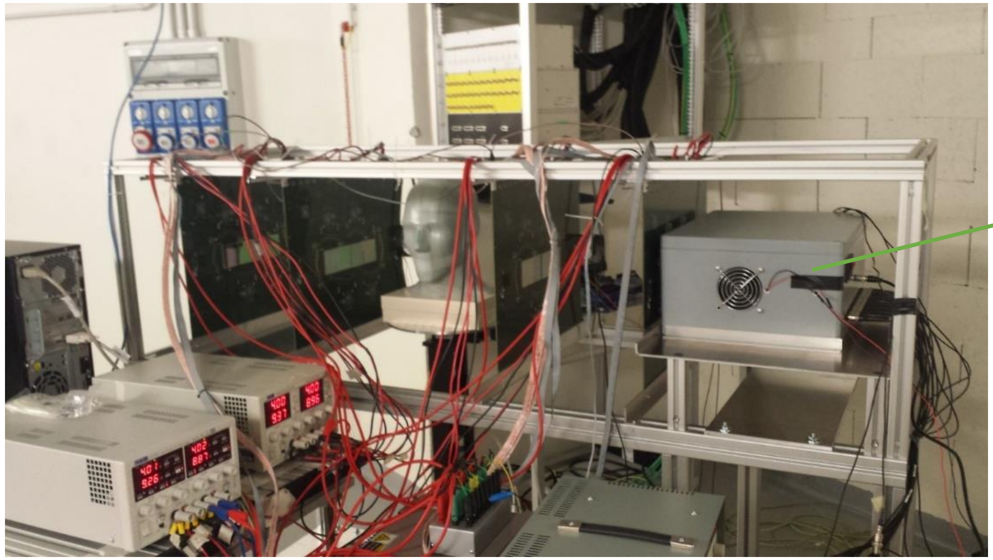
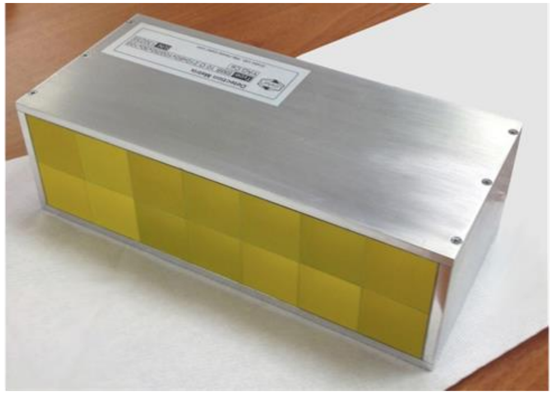
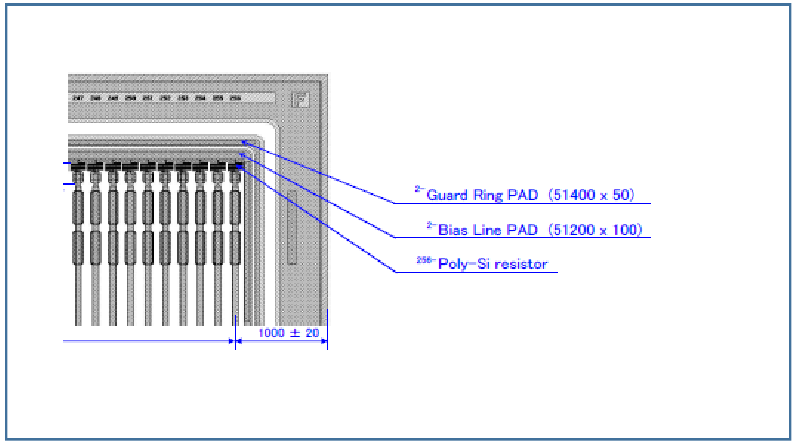


Calorimeter



2x7 YAG:Ce Crystals Array
$3x3x10cm^3$ each
Read-out by Silicon photodiodes



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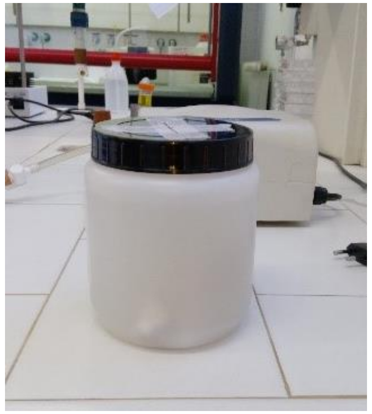
RSP measurements in clinical practice

- Presently no pCT apparatus certified for use on patient exists
- stopping power maps are calculated starting from the HU maps measured by a xCT scan, thus requiring a HU – RSP conversion
- Single-energy x-CT calibration is obtained by scanning a number of tissue equivalent materials (TEMs), suffering limitations in mimicking the properties of real tissues.
- To partially overcome that issue, a stoichiometric calibration has been proposed or, more recently, dual-energy x-CT methods were investigated.
- These are ‘two steps’ processes:
  1. x-CT scan to compute relative electron or mass densities (for DECT also the effective atomic number is computed);
  2. translation of such quantities into proton RSP using a heuristic function, which depends on specific material related properties affected by large experimental errors such as the mean excitation energy.

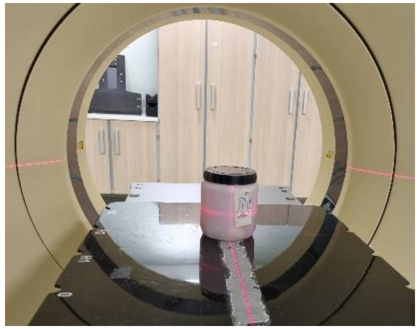
The XP-Calib project: xCT calibration by pCT

- reduce errors in xCT calibration by using pCT to **directly measure** RSP maps of test phantoms
- Use **biological materials** to better reproduce human tissue properties
- One phantom imaged by xCT and pCT systems
- HU (from xCT) are '*correlated*' to SPR (from pCT), pixel-wise, to obtain the calibration function

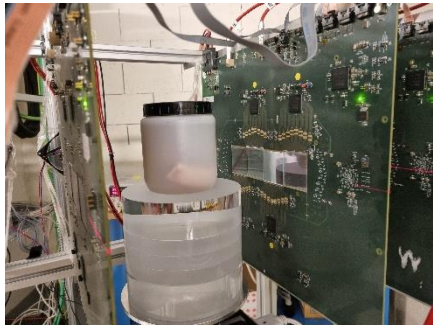


Biological phantom

xCT



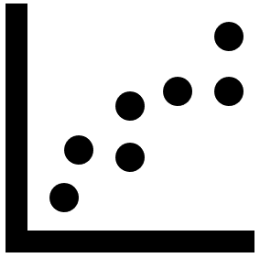
pCT



HU

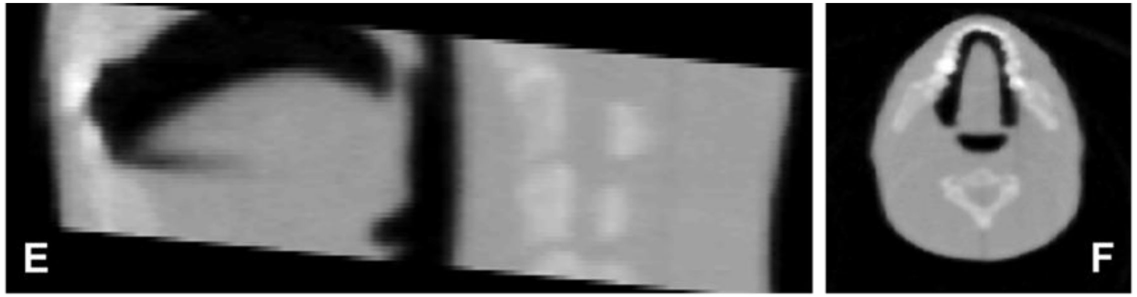
SPR

$$SPR(x,y,z) = \boldsymbol{f}(HU(x,y,z))$$

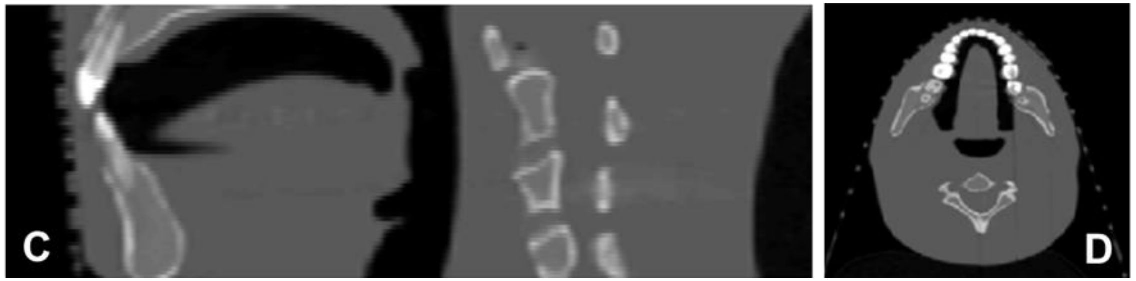


xCT calibration procedure

- Acquire pCT and xCT images of the same phantom
- Register the two images
- Build a scatter plot RSP vs HU and extract best correlation curve

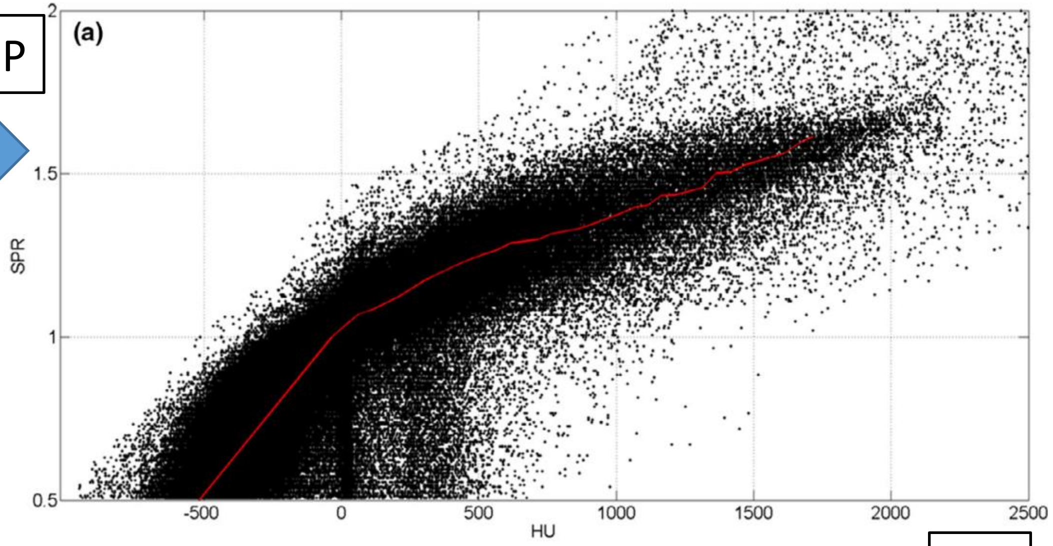


pCT image



xCT image

RSP

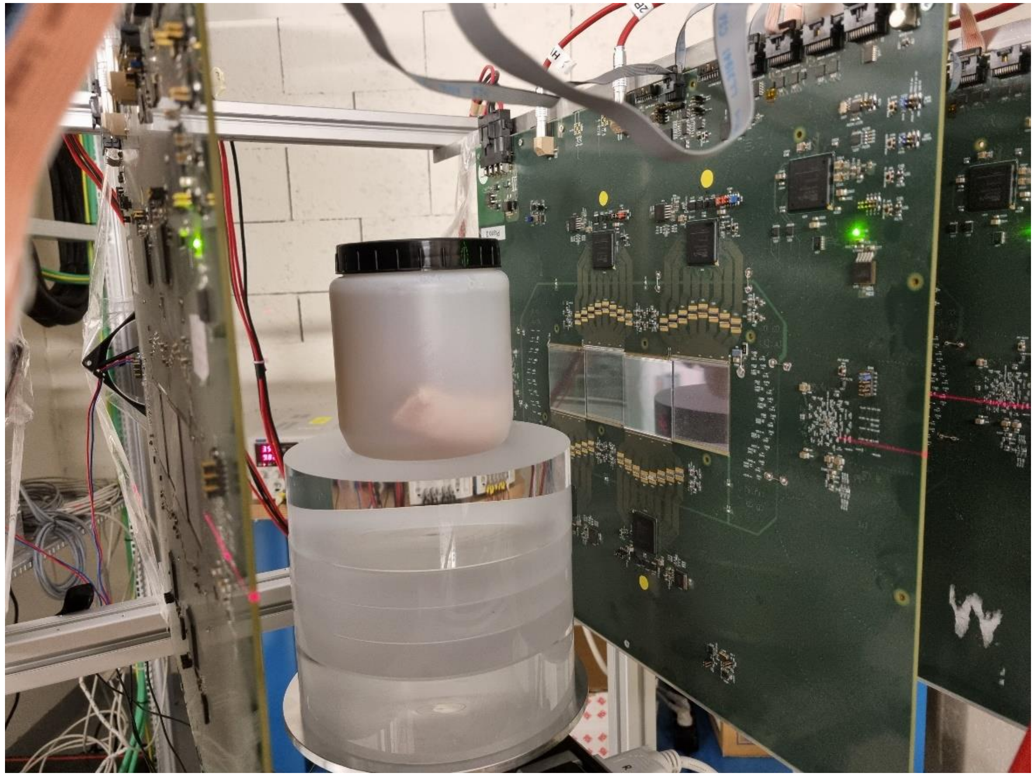


HU

Technical Note: CT Calibration for Proton Treatment Planning by Cross-Calibration with Proton CT Data

Paolo Farace *et al.* 2020 *Med. Phys.* In press.
[https://doi.org/10.1002/mp.14698]

Biological phantom



The stabilized bio-phantom inserted in the pCT apparatus

Beef cutlet

A histology stabilization protocol has been used to stabilize the tissues preserving their physical features:

- Fixation by buffered formalin
- Rinsing by deionized water
- Vacuum degassing

A gel-forming polysaccharide with a low gellification temperature has been used to coat the tissue with a rigid aqueous matrix

10% w/v Agar-Agar solution, activation at 95-100°C, then cooling at 40-45°C

The tissue is stabilized, immersed in the activated Agar-Agar solution at 40°C, then cooled at RT

The stabilization procedure allows to ship the phantom to remote proton therapy center for xCT scanner calibration

INFN pCT apparatus tuning

For optimal image quality particular care has to be given to all instrumental aspects influencing spatial resolution and RSP accuracy and resolution:

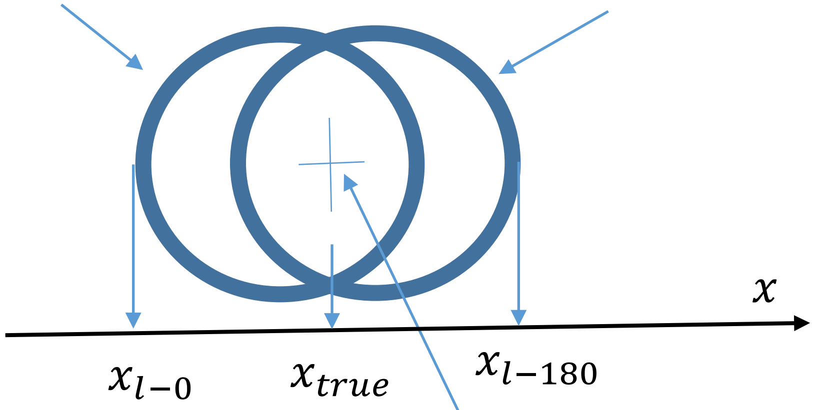
- Tracker alignment
- Energy calibration
- Energy reconstruction

pCT tuning: tracker alignment

Tracker planes are aligned by globally minimizing the trajectory residuals while applying shift and rotations to the measured coordinates of all the planes except a reference one

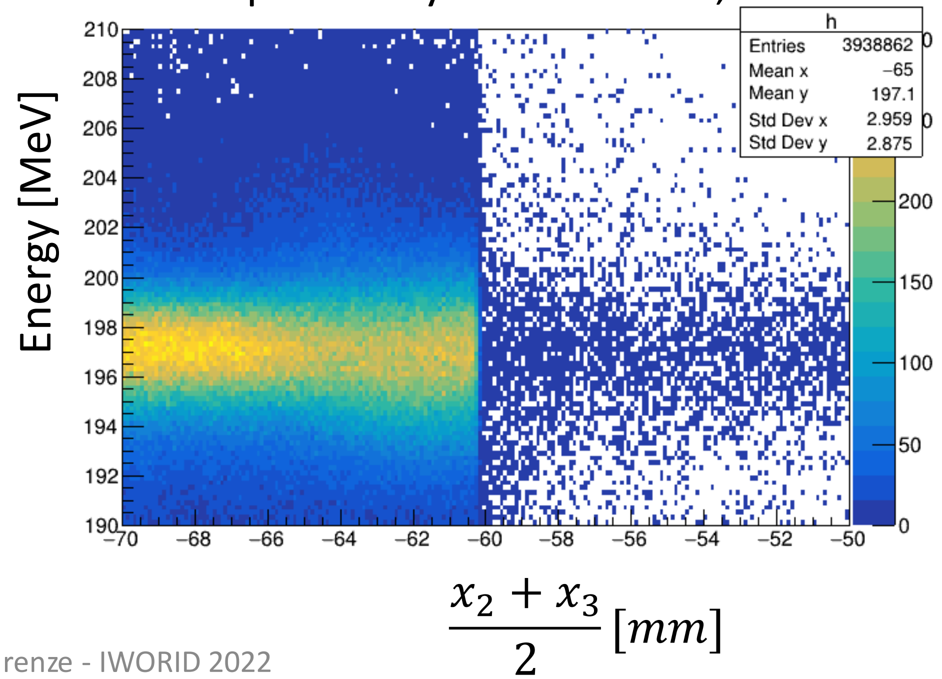
After the relative alignment is done, the position of the rotation axis in the global tracker reference system is determined:

2 radiographies of a brass cylinder $2x10^7$ events each



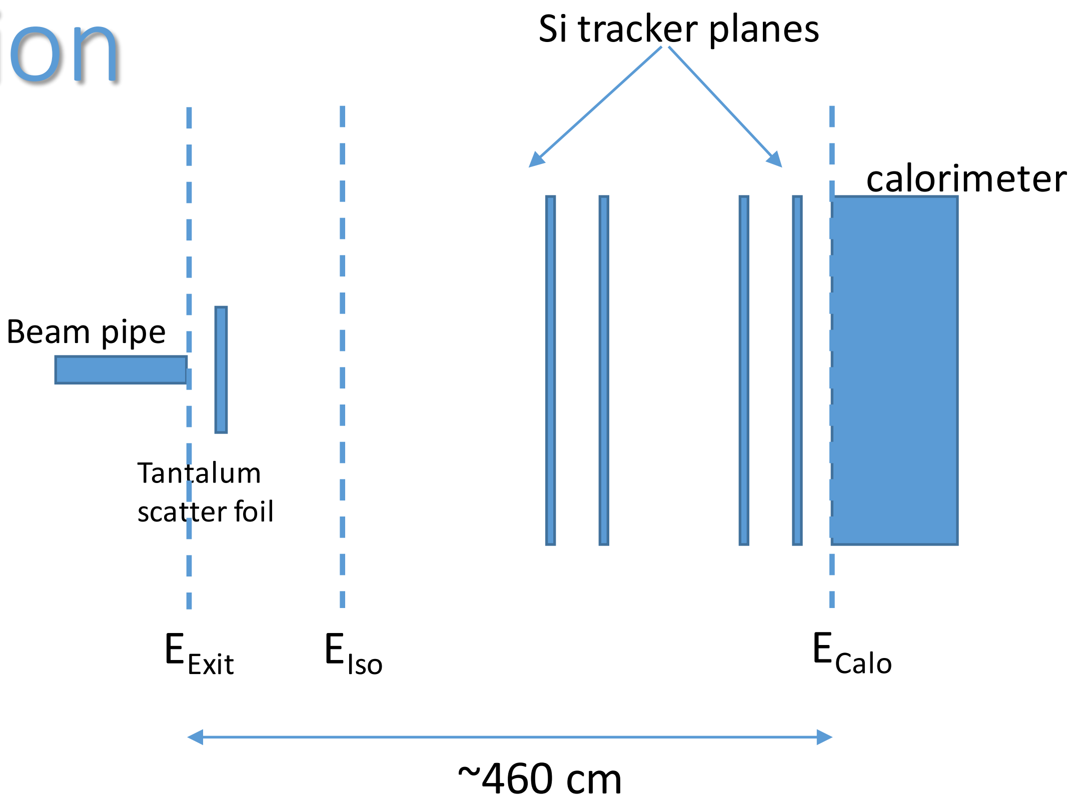
$$x_{true} = \frac{1}{2}(x_{l-0} + x_{l-180})$$

Example of a cylinder shadow,

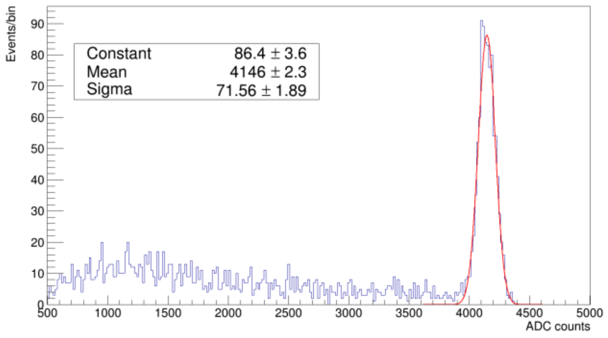


pCT tuning: Energy calibration

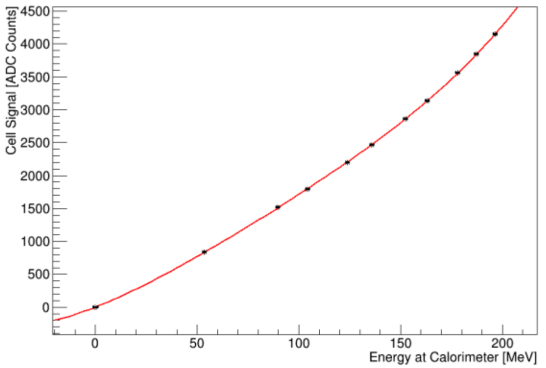
- 10 calibration runs with no phantom, E_{iso} [1] ranging from 80 to 210 MeV
- E_{Iso} values reported back to E_{exit} using air SP from NIST PSTAR[2]
- E_{calo} calculated with GEANT4 simulations
- Calorimeter divided in 1.5x1.5 cm^2 bins, 1 calibration curve per bin



Gaussian fit for one bin



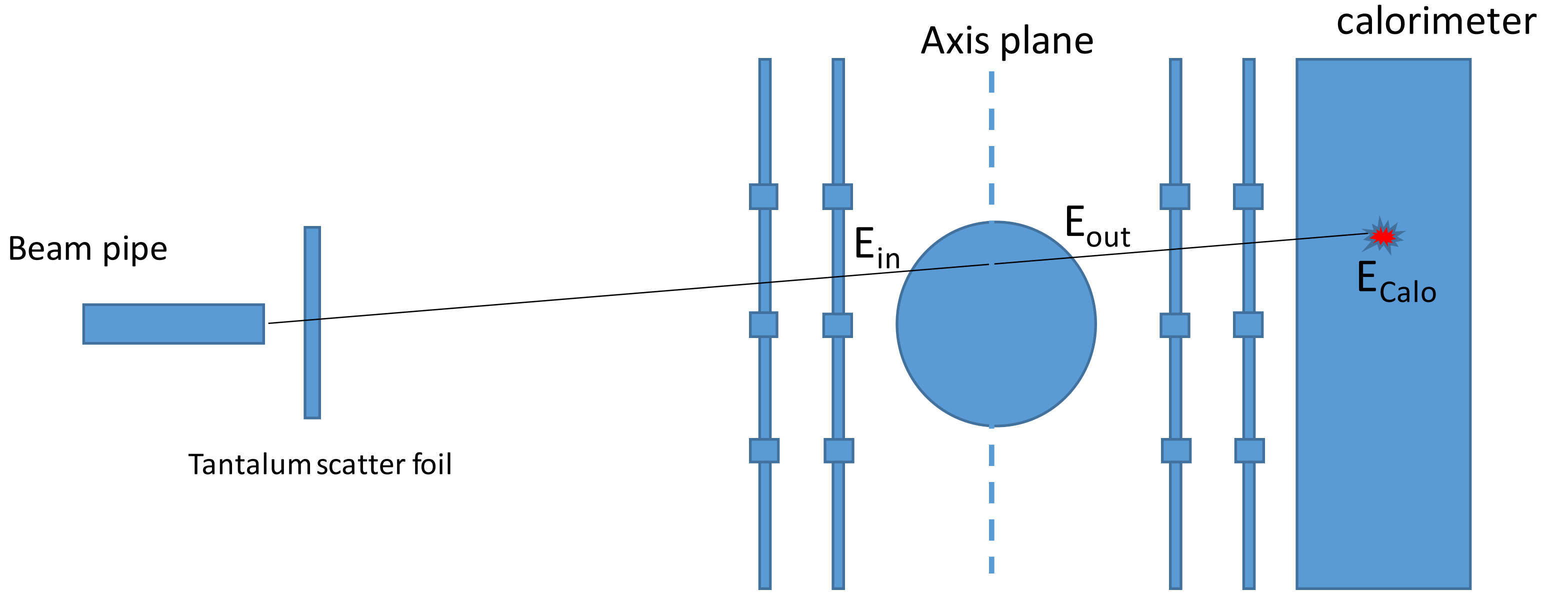
Calibration curve with polynomial fit



E_{ISO} [MeV]	E_{Exit} [MeV]	E_{Calo} [MeV]
82.3	83.402	52.687
111.2	112.08	88.908
124.1	124.91	103.73
141.7	142.44	123.34
152.7	153.40	135.32
168.1	168.76	151.87
178.2	178.83	162.62
192.3	192.90	177.51
201.1	201.69	186.74
210.0	210.57	196.04

[1] Tommasino et al., Nucl. Instrum. Methods Phys. Res. A, 869 (2017)
[2] https://physics.nist.gov/PhysRefData/Star/Text/PSTAR.html

pCT tuning: Energy reconstruction

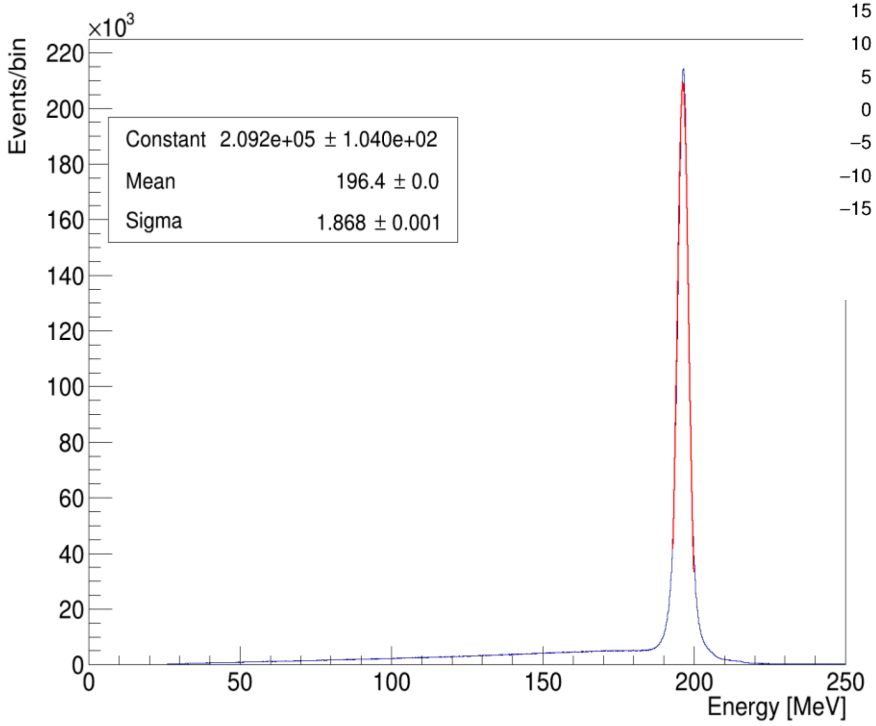


E_{in} calculated by GEANT4 simulation taking into account the geometry of the detector
$E_{out} = E_{calo} + \Delta E_{Si} + \Delta E_{air}$

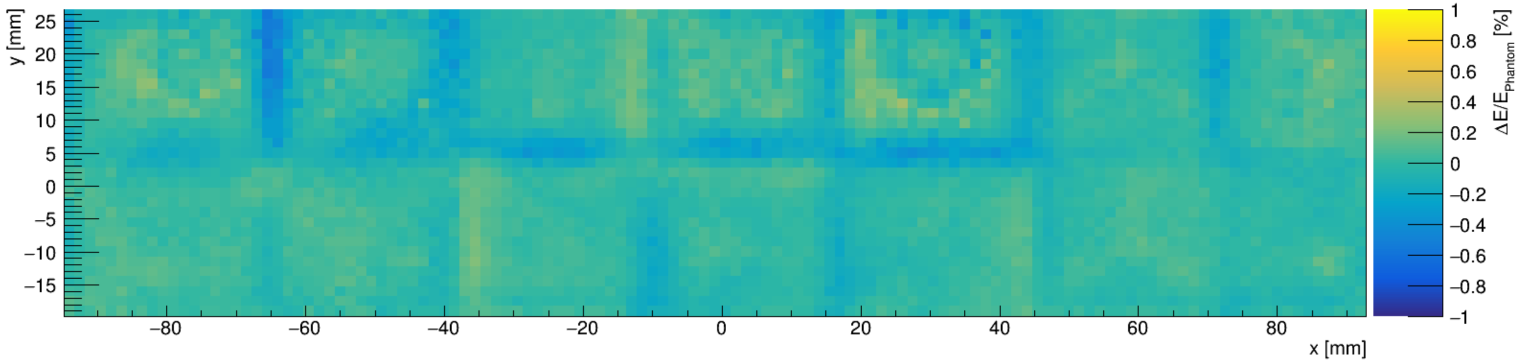
ΔE_{Si} , ΔE_{air} are computed using the NIST stopping power tables

E_{in}, E_{out} corrected event by event for possible additional energy loss in Si overlaps

Energy resolution and uniformity



Overall resolution < 1% @ 200 MeV

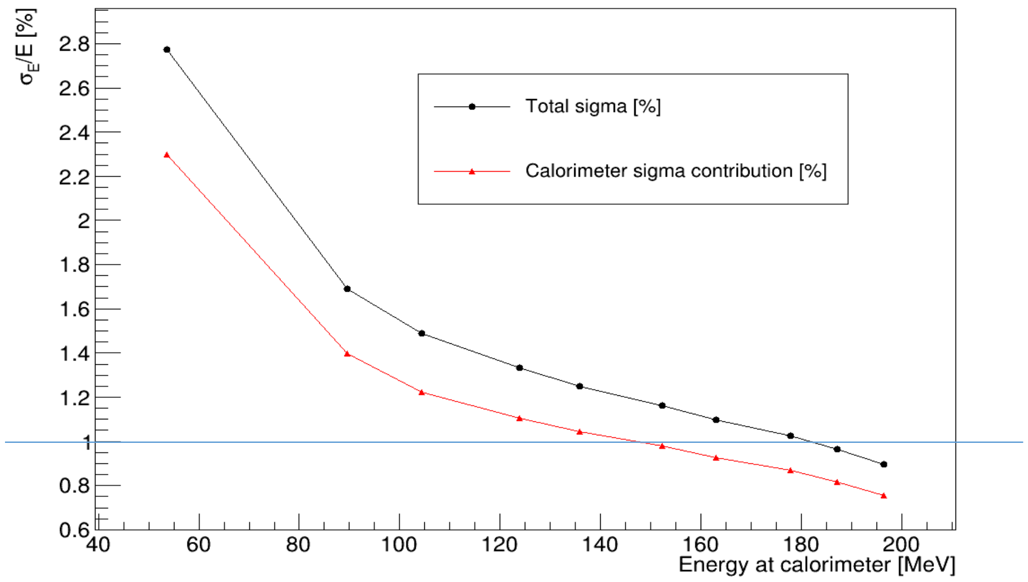


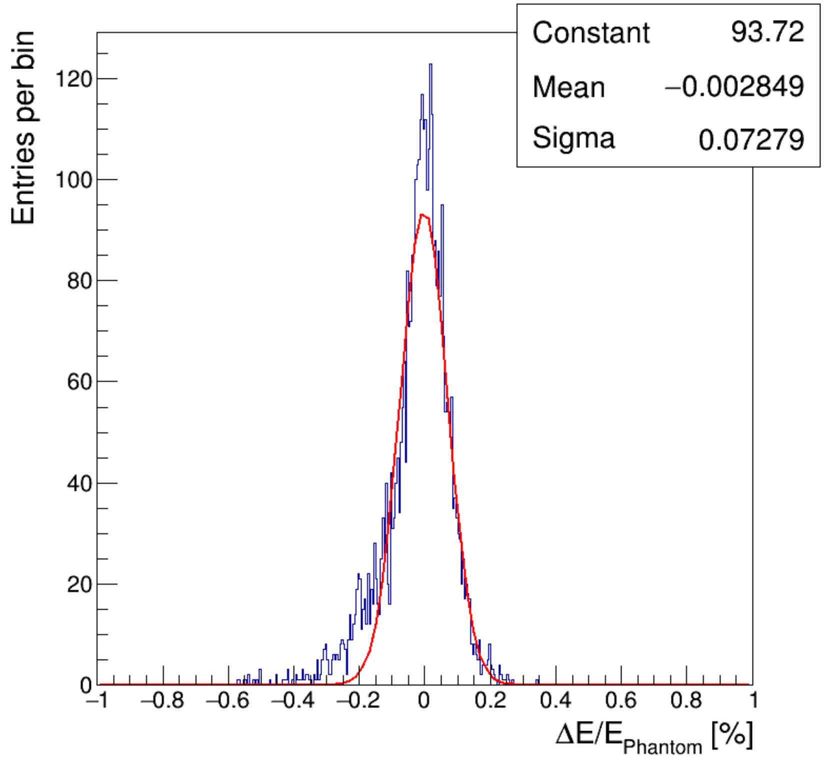
$\Delta E = E_{out}^{axis} - E_{in}^{axis}$

E_{out}^{axis} : E_{calo} measured **value** reported at phantom plane using SP values of transversed materials

E_{in}^{axis} : simulated vaue at phantom plane

Energy resolution and uniformity





$\Delta E = E_{out}^{axis} - E_{in}^{axis}$

Total sigma includes contribution from accelerator energy spread and Tantalum

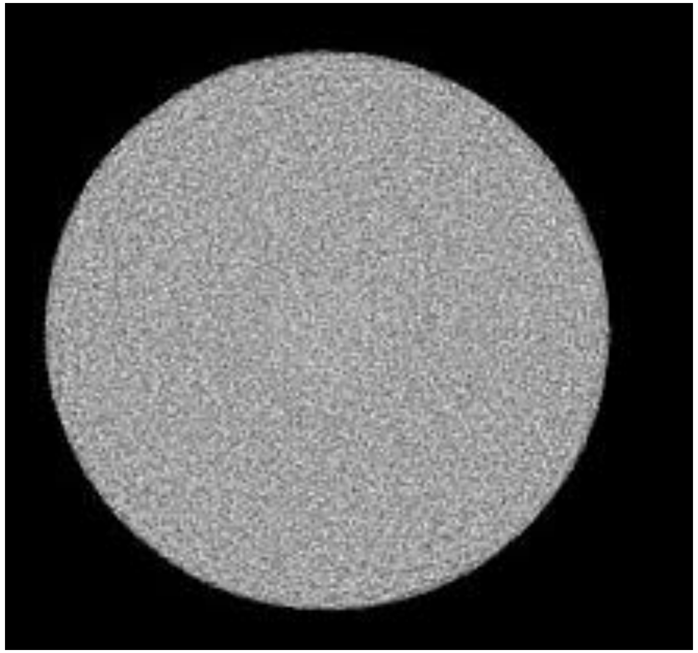
Overall resolution < 1% @ 200 MeV

E_{out}^{axis} : E_{calo} measured **value** reported at phantom plane using SP values of transversed materials

E_{in}^{axis} : simulated vaue at phantom plane

PCT verification: water tomographies

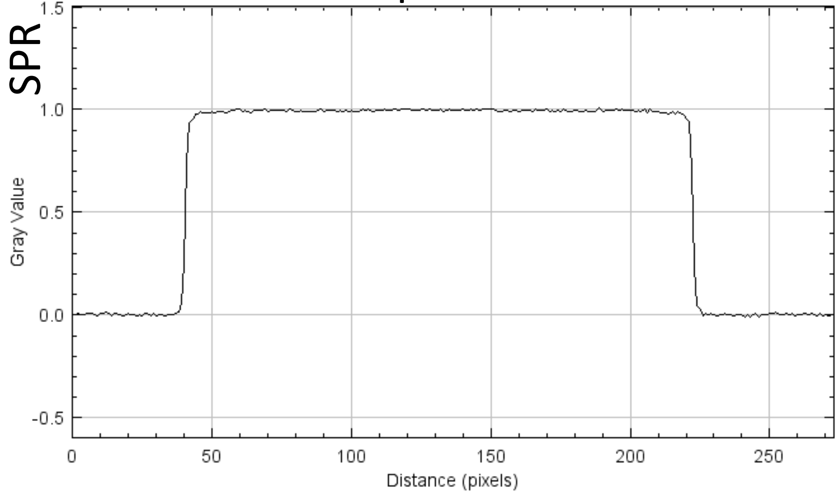
- All images shown in this presentation are reconstructed using anopen-source reconstruction algorithm (Filtered Backprojection along Most likely paths [1]) developed by Simon Rit group at CREATIS Research Lab, Lyon



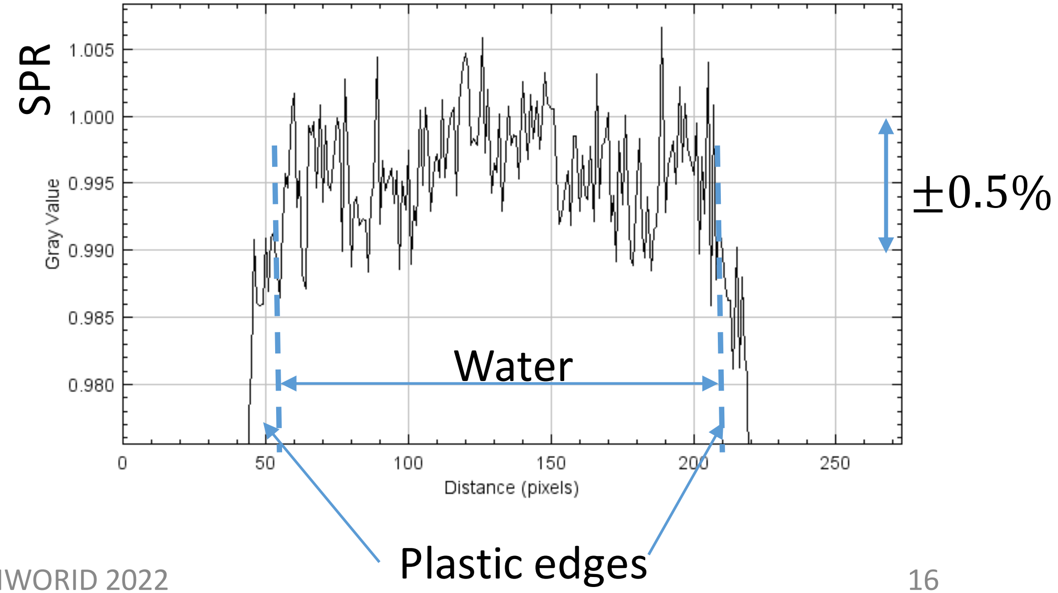
Single axial slice of a 115mm diameter water phantom

[1] Simon Rit et al. "Filtered backprojection proton CT reconstruction along most likely paths" Med Phys 40(3), March 2013

SPR profile



zoom



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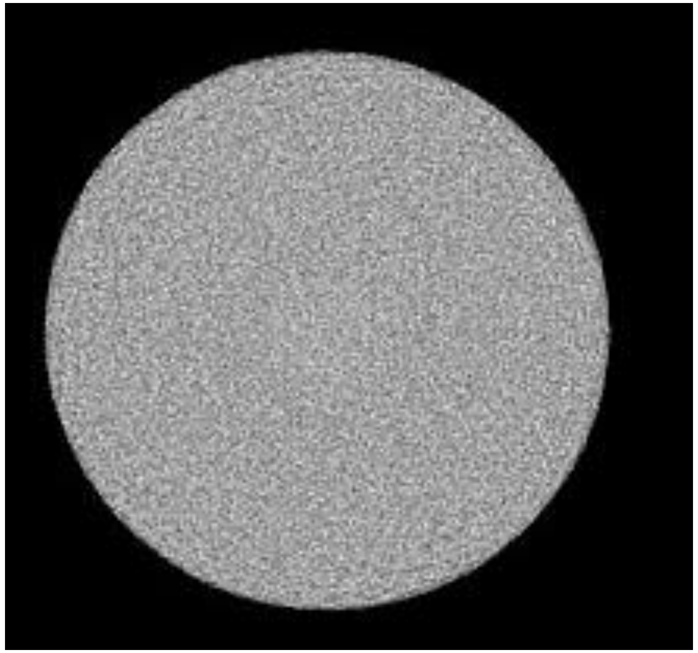
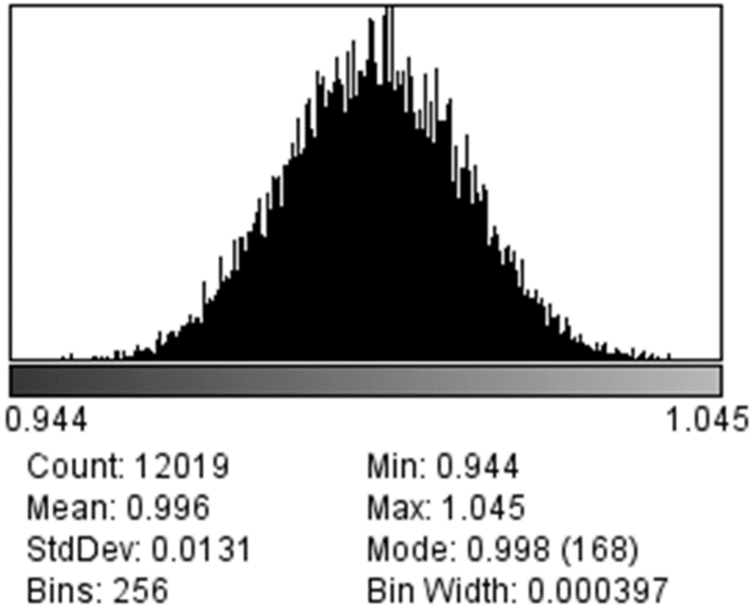


Single axial slice of a 115mm diameter water phantom

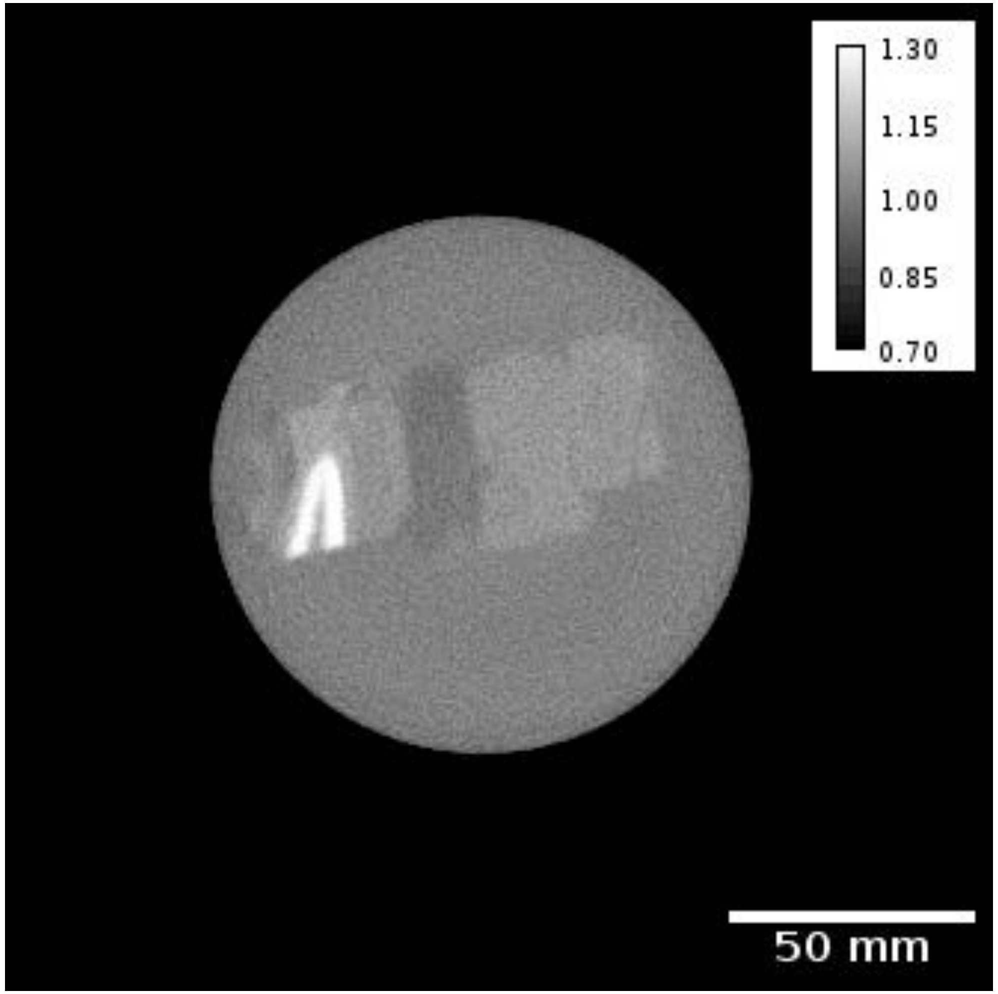
SPR distribution
(plastic edges excluded)



Uniformity and precision about ± 5 *per mille*

[1] Simon Rit et al. "Filtered backprojection proton CT reconstruction along most likely paths" Med Phys 40(3), March 2013

Tomographic images: bovine phantom



Stabilized bovine phantom, 115 mm diameter
Axial view tomography
pixel: 0.6x0.6x2.75 mm^3
$6x10^8$ protons
Entrance energy ~197 MeV

xCT acquired on the same phantom, cross-calibration analysis in progress

Conclusions

- A novel method of xCT calibration for treatment planning in proton therapy using pCT has been proposed
- A characterization of the pCT apparatus has been carried out showing an energy resolution <1% and uniformity ± 0.5% @200 MeV proton beam energy
- Phantoms composed of stabilized biological samples have been produced and imaged
- xCT calibration analysis is under way