A pCT approach to CT calibration in proton therapy treatment planning

Mara Bruzzi[1,2], Paolo Farace[3,4], E. D'Amato[4,5], Elena Fogazzi[3,5], Francesco Fracchiolla[3,4] Stefano Lorentini[3,4], Roberto Righetto[3,4], Monica Scaringella[1], Marina Scarpa [3,5], Francesco Tommasino[3,5], Diego Trevisan[6] and Carlo Civinini[1]

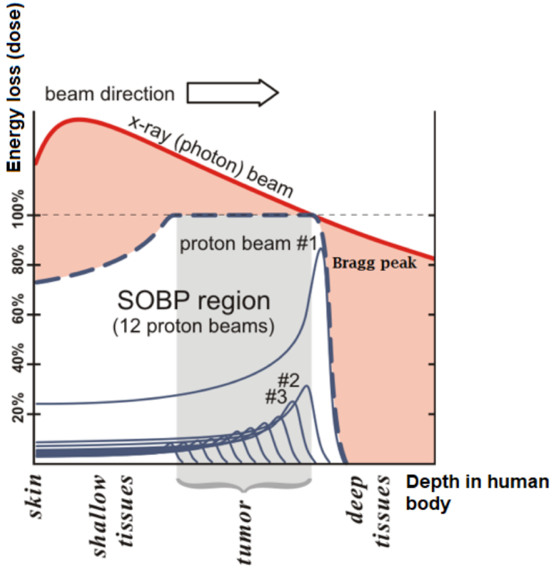
[1] Florence Division of INFN National Institute for Nuclear Physics , Sesto Fiorentino (FI), Italy
[2] Physics and Astronomy Department, Florence University, Sesto Fiorentino (FI), Italy
3 Trento Institute for Fundamental Physics and Applications (TIFPA), Trento division of INFN, Povo (TN), Italy
[4] Proton Therapy Unit, Hospital of Trento, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy
[5] Physics department, Trento University, Povo (TN), Italy
[6] Medical Physics Department, Hospital of Trento, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy

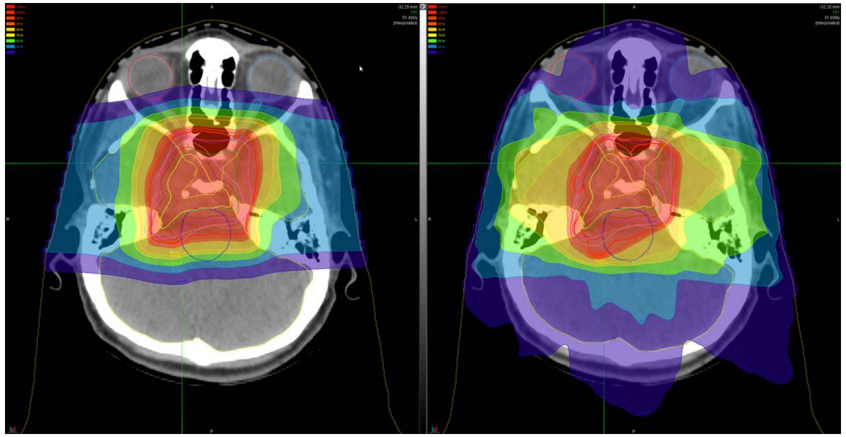
Outline

- ❑ Background and motivation for proton Computed Tomography (pCT)
- ❑ Short review of pCT activity in Italy
- ❑ Results on proton tomography reconstruction with non-homogeneous phantoms
- ❑ Ongoing research on X-CT vs pCT cross-correlated calibration
- ❑ Conclusions

Why proton Computed Tomography?

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





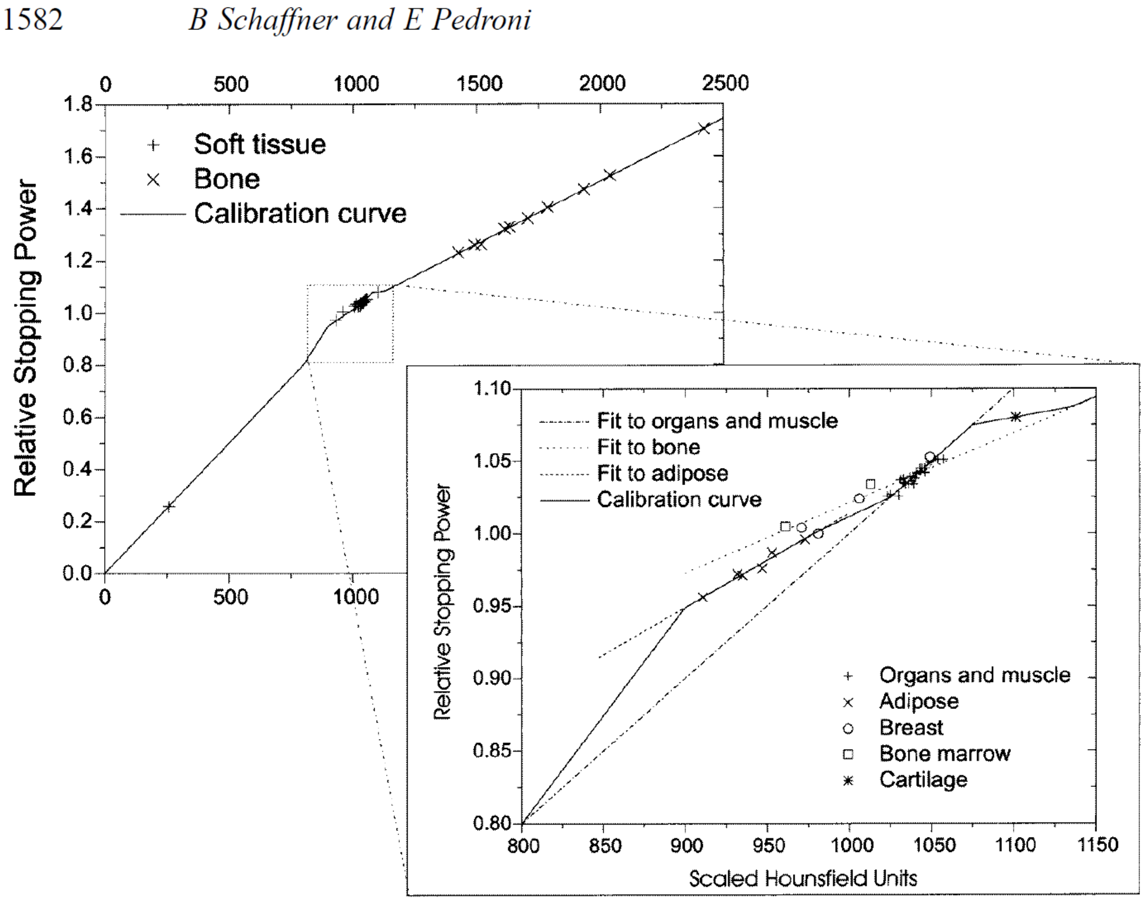
Treatment plans dose comparison

The measurements of the amount of material in front of the tumor is of paramount importance to set the correct proton beam energy.

To this purpose treatment planning programs presently use proton stopping power maps derived from x-ray attenuation coefficients (Hounsfield Units – HU) resulting in errors on Bragg peak position up to *a few millimeters*.

A **proton based CT** could **directly measure** the 3D proton relative stopping power maps (RSP) eventually reducing inaccuracies in tumor irradiation.

Hounsfield Units Vs Relative Stopping Power



B. Schaffner and E. Pedroni Phys. Med. Biol. ***43 (1998) 1579–1592***

The proton range error due to the HU/RSP conversion depends on the tumor depth and the tissues crossed by the beam and could be as large as ~3 mm.

If protons are used to directly determine the RSP maps this error contribution could be eliminated.

Table 1. Two typical proton treatment cases and expected range errors. The expected error in the position of the distal fall-off of the dose distribution is expected to be a few millimetres in typical cases of proton therapy.

	Soft tissue			Bone			
	Amount (cm)	wer[a] (cm)	Abs. error (cm)	Amount (cm)	wer[a] (cm)	Abs. error (cm)	Total Abs. error (cm)
Brain	10	10.3	0.11	1	1.8	0.03	0.14
Prostate (lateral beam)	15	15.5	0.17	5	9	0.16	0.33

[a] Water equivalent range.

Range uncertainties in proton therapy

Potentially reduced by pCT

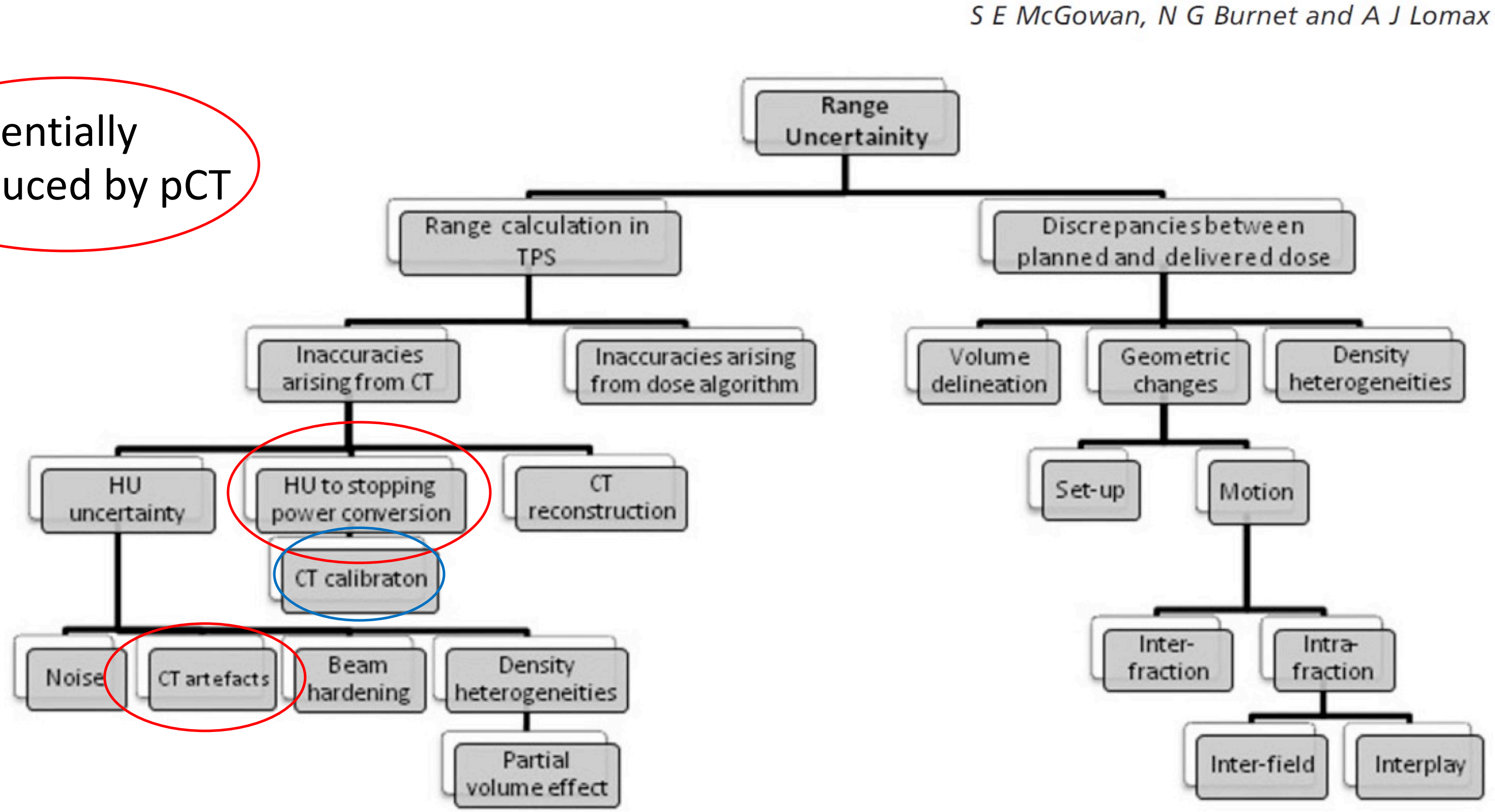


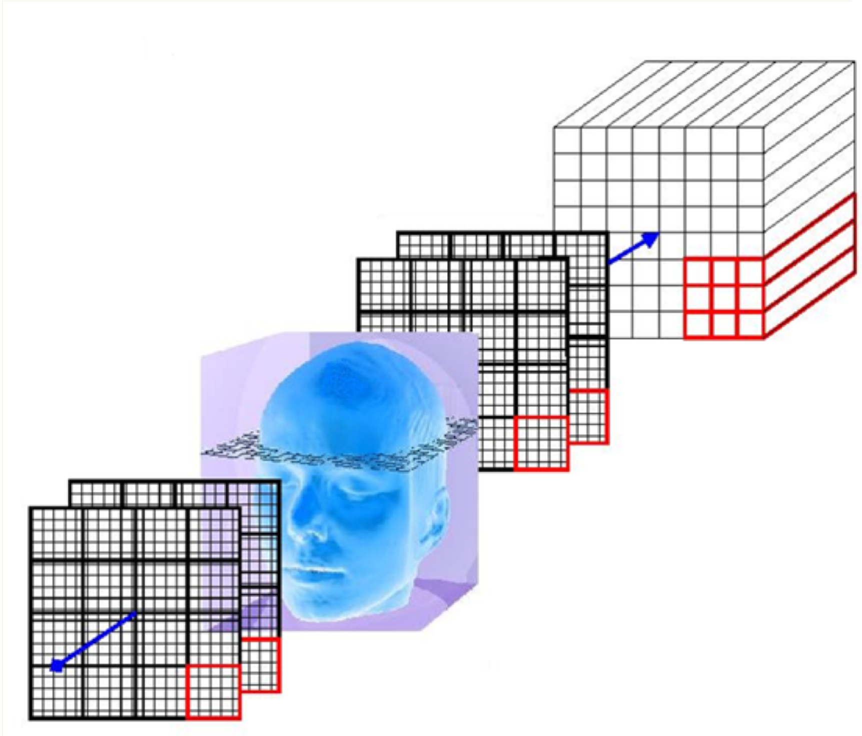
Figure 2. Schematic of sources of range uncertainties in proton radiotherapy. HU, Hounsfield unit; TPS, treatment planning system.

McGowan SE, Burnet NG, Lomax AJ. Treatment planning optimisation in proton therapy. Br J Radiol 2013;86:20120288.

How to perform a proton computed Tomography?

Use a **monoenergetic proton beam** able to cross the patient's body (200-230 MeV): the residual proton energy (or range) carries information about the **stopping power distribution** of the traversed material.

Phantom rotated during data taking to collect protons entering the object from many different (ideally continuous) directions.



To mitigate the effect of the multiple Coulomb scattering we need an ***event-by-event*** measurement:

1) **Tracker** to measure coordinates and direction of each proton to estimate the Most Likely Path (MLP)
2) **Calorimeter** to assign an energy loss to each proton track
3) **Image reconstruction** → Most Likely Path + Algebraic or FBP* algorithms running on GPUs .

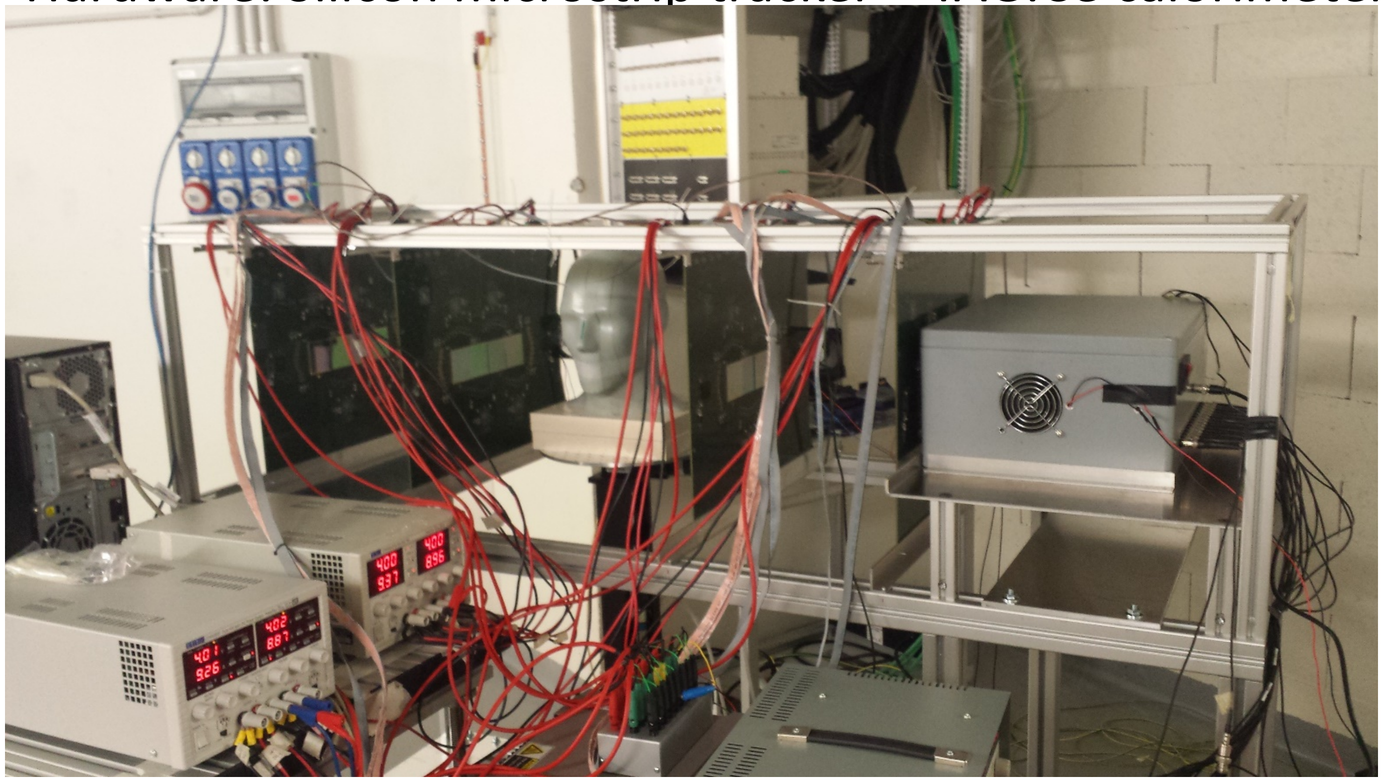
* Simon Rit, George Dedes, Nicolas Freud, David Sarrut, and Jean Michel Létang Filtered backprojection proton CT reconstruction along most likely paths Med. Phys. 40 (3), March 2013

The INFN-pCT apparatus

Manufactured by INFN-Florence and Catania (2014 – 2017) running since 2018

Now installed in operation at the Trento proton therapy center's experimental beam line

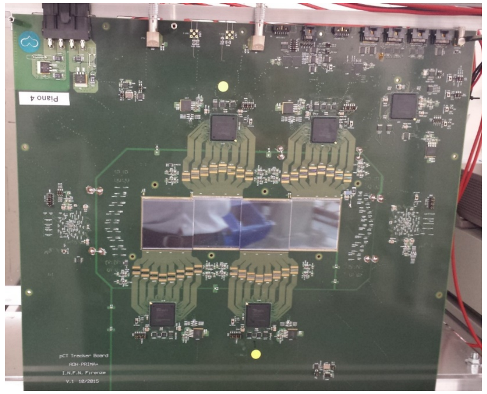
Hardware: Silicon microstrip tracker + YAG:Ce calorimeter

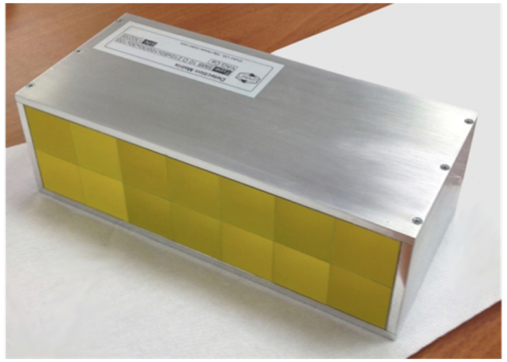


INFN pCT system under test with an anthropomorphous head phantom at Trento proton therapy center's experimental beam line

Silicon microstrip tracker 5x20cm² field of view

- 4x2 silicon microstrip detectors 200μm pitch, 320μm thick active area 5x20cm²
- front-end chips and 2 levels FPGA





Calorimeter

- 2x7 YAG:Ce crystals 3x3x10 cm^3 ; 70 ns scintillating light decay time
- photodiodes + Analogue amplifier + shaper (1μs)

<1% energy resolution @ 200 MeV

Electron density phantom

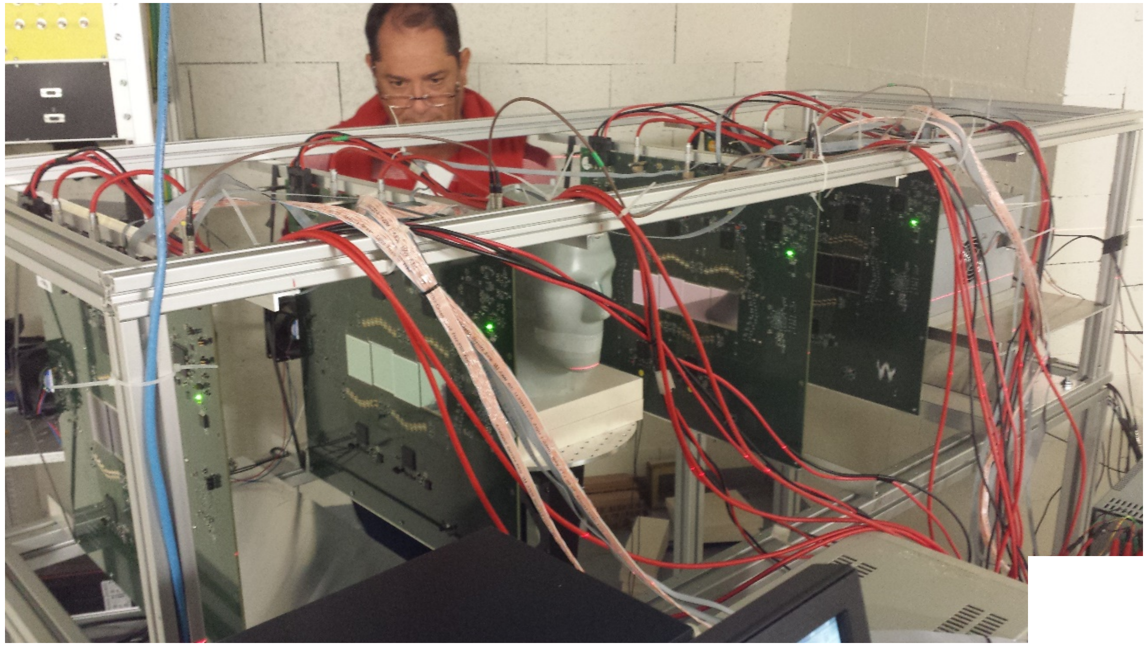
→8 lateral plugs:

1) Liver 1.07 gcm^{-3}
2) Lung exhale 0.50 gcm^{-3}
3) Breast 0.99 gcm^{-3}
4) Bone 1.53 gcm^{-3}
5) Muscle 1.06 gcm^{-3}
6) Bone 1.16 gcm^{-3}
7) Adipose 0.96 gcm^{-3}
8) Lung inhale 0.20 gcm^{-3}

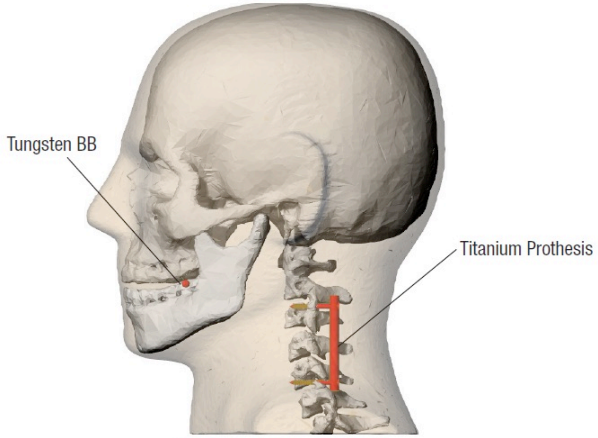
→Central plug:
Liquid water vial

→All of them embedded into a 'water equivalent' plastic material (Plastic Water LR)

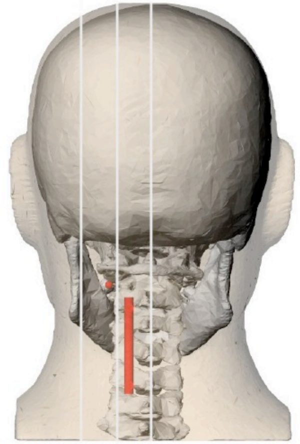
Anthropomorphous phantom



CIRS Proton Therapy dosimetry head. Mod. 731 HN



Model 731-HN Sagittal Rendering

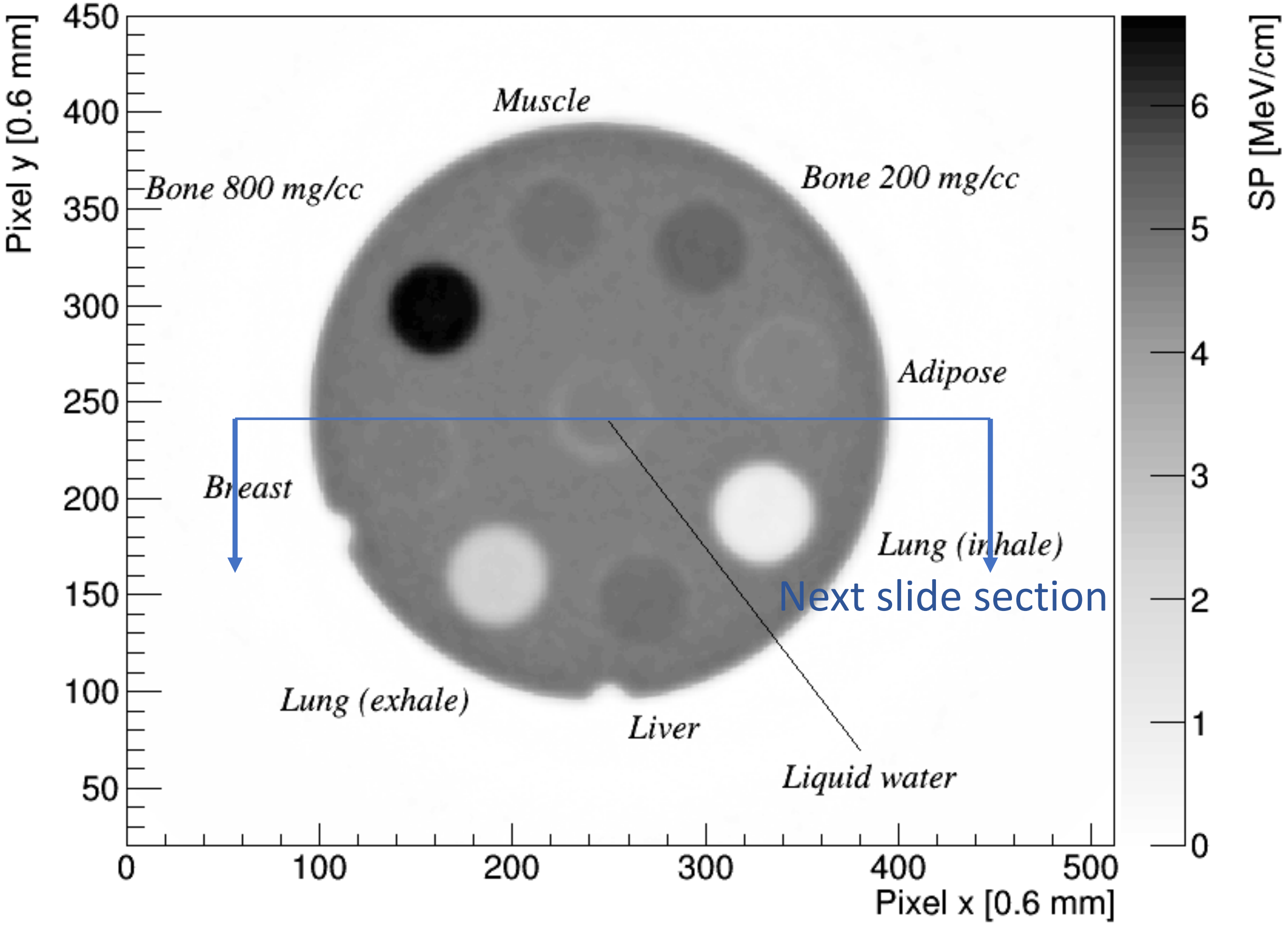

Back view of phantom with sagittal cuts

Data Acquisition Procedure

- Data collected @ experimental beam line of the Trento Proton Therapy Centre

- Energy scan for calorimeter calibration and alignment (no phantom)
  - Calibration: 6-10 energies 1-2x10^7 events between 83-211 MeV
  - Alignment run 1-2x10^7 events @ 211 MeV
- Two sets of data for tomography reconstruction
  - Electron density phantom ~ 10^8 events in 400 angles
  - Anthropomorphic phantom ~ 1.2x10^8 events in 400 angles

a. Electron density phantom tomography



1.6mm thick central slice of the tomography

Radial artefacts eliminated by decreasing angular steps (0.9°)

Algebraic reconstruction with MLP: 75th iteration →long time processing

- All tissue substitute inserts visible

- Quantitative analysis → next slides

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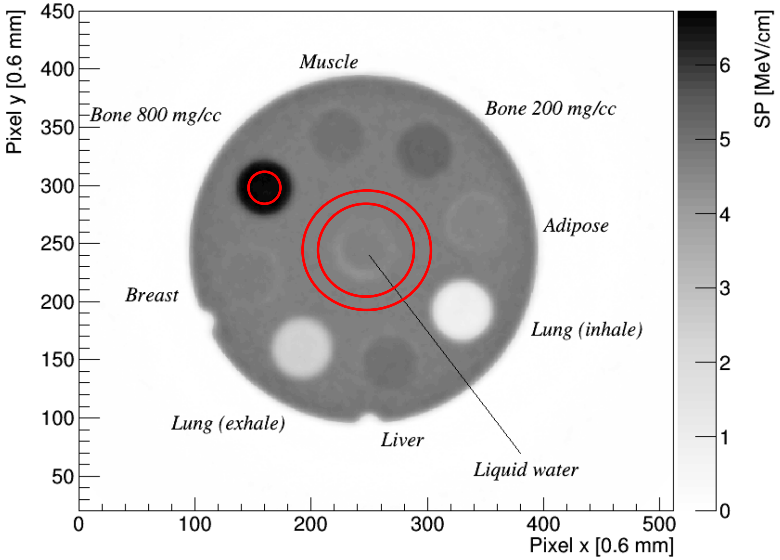
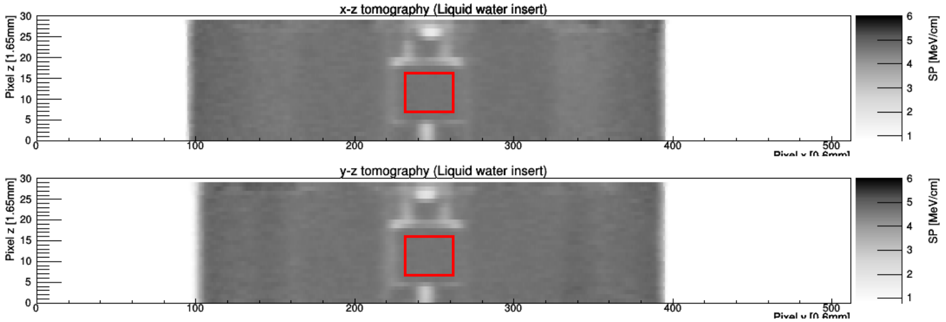
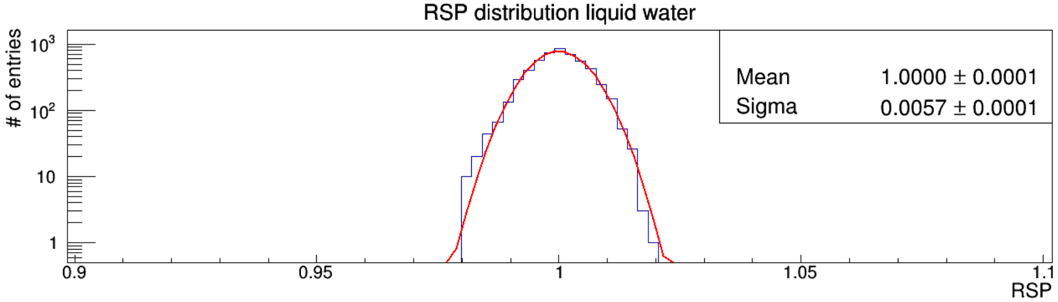
Electron density phantom tomography



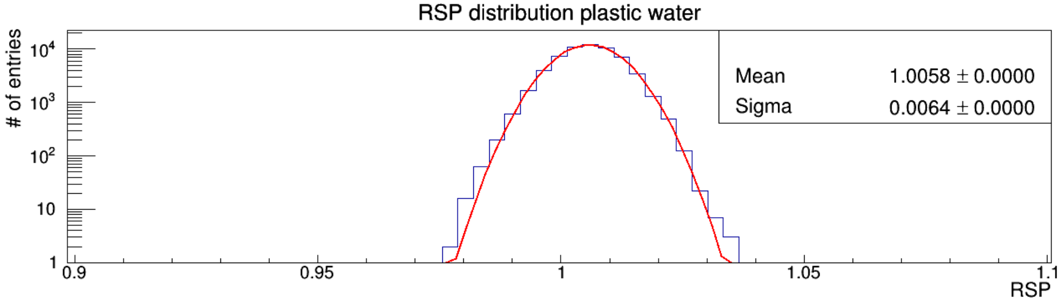
Distilled water vial used to normalize the Stopping Power values obtaining the Relative Stopping Power.



Red: fiducial regions to define RSP values



RSP of distilled water σ = 0.6%



Measured RSP of the Plastic Water is 1.0058 (expected value 1.008) σ = 0.6%

Presently not needed (improved calibration – see C. Civinini talk)

Expected RSP calculated/measured

Expected RSP calculated using Geant4 simulation using the G4EmStandardPhysics_option3 dataset recommended for medical Physics applications.

Tissues substitutes elemental composition and density inserted into Geant4 and SP values @180MeV extracted.

Materials RSPs measured using MLIC (multi layer ionization chamber) directly on the proton beam (last column).

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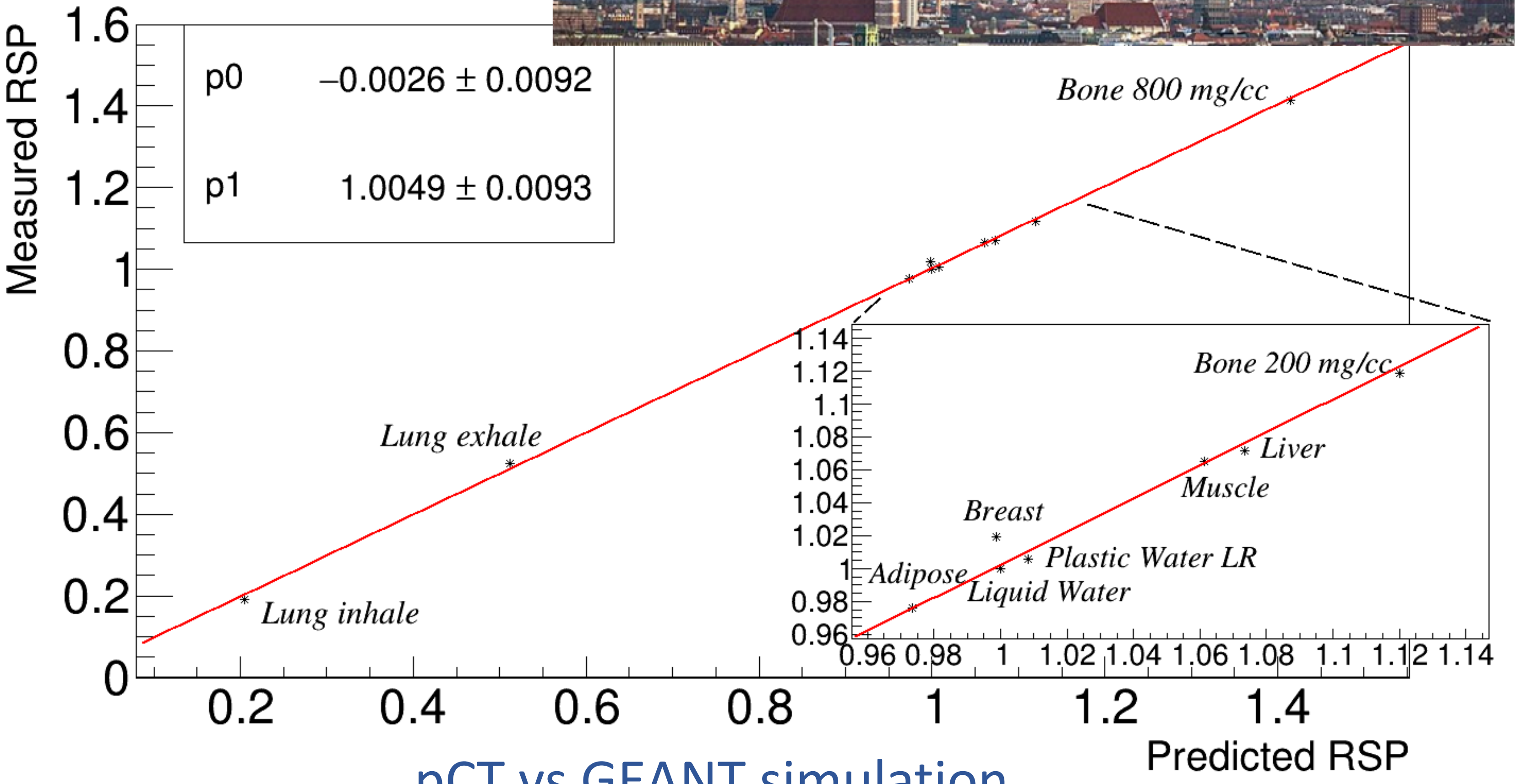
Electron density phantom (CIRS 062M) material density, expected SP and RSP values for 180 MeV protons, and MLIC-measured RSP.

Material	Density g/cm^3	Geant4 SP MeV/cm	Geant4 RSP	MLIC-measured RSP
Lung (inhale)	0.205	0.979	0.204	0.26
Lung (exhale)	0.507	2.449	0.511	0.54
Adipose	0.96	4.655	0.971	0.96
Breast	0.99	4.775	0.996	1.02
Distilled Water	1	4.792	1	-
Plastic equiv. water	1.029	4.822	1.006	-
Muscle	1.06	5.076	1.059	1.06
Liver	1.07	5.133	1.071	1.06
Bone (trabecular)	1.16	5.357	1.118	1.40
Bone (dense)	1.53	6.767	1.412	1.12

RSP correlation

Material	pCT-measured RSP (mean)	pCT-measured RSP (sigma)	pCT-MLIC RSP relative difference [%]	pCT-Geant4 RSP relative difference [%]
Lung (inhale)	0.192	0.009	-35.6	-6.53
Lung (exhale)	0.526	0.009	-3.15	2.40
Adipose	0.976	0.008	1.62	0.47
Breast	1.017	0.009	-0.26	2.06
Distilled Water	1	0.006	-	-
Plastic equiv. water	1.006	0.006	-	-0.05
Muscle	1.065	0.008	0.44	0.52
Liver	1.070	0.010	0.97	-0.06
Bone (trabecular)	1.118	0.008	-0.20	-0.003
Bone (dense)	1.414	0.009	0.96	0.11

pCT vs MLIC



pCT vs GEANT simulation

Mean absolute percentage error (MAPE) excluding lung inserts (2020):

- **pCT/MLIC 0.74%**
- **pCT/Geant4 0.54%**

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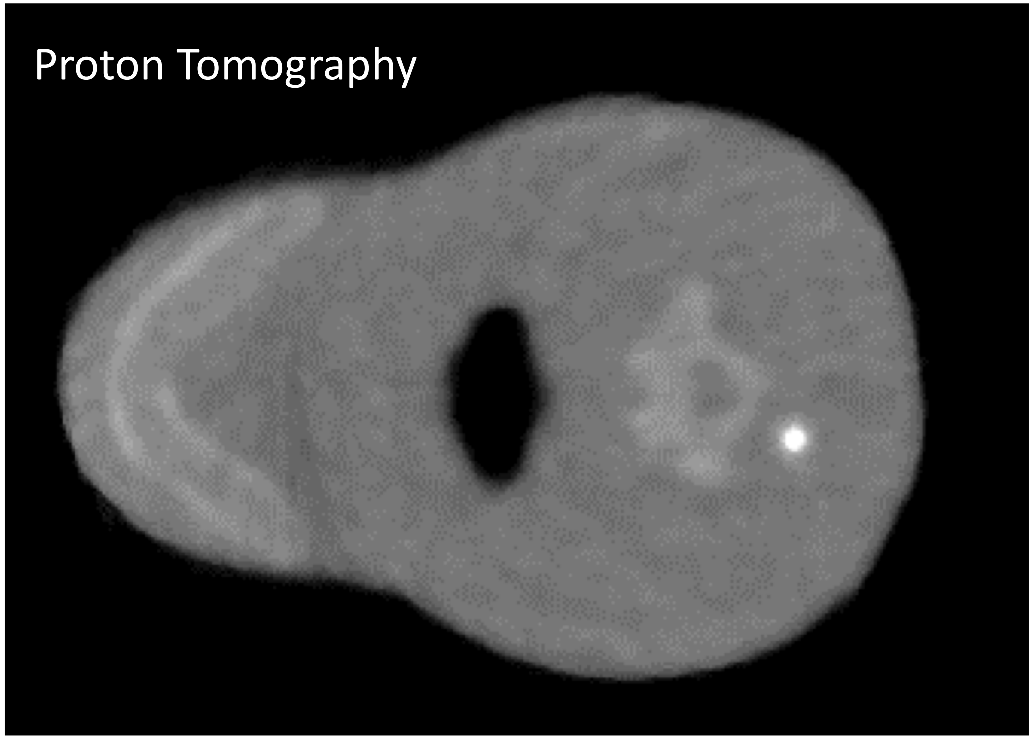
See **E. Fogazzi talk tomorrow** for new results about increased RSP precision obtained after a more accurate calibration method (see C. Civinini talk)

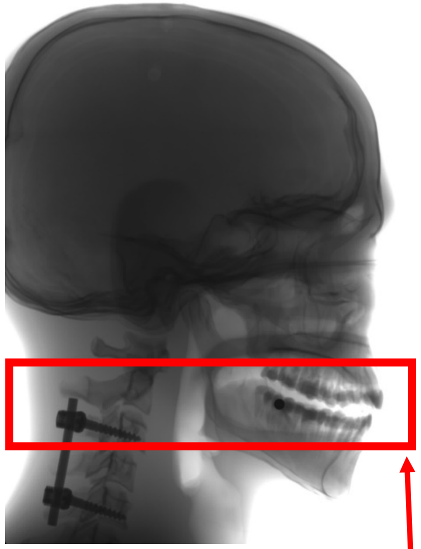
b. Anthropomorphous phantom head proton tomography

- Head phantom proton tomographies taken at APSS-Trento proton therapy center with the pCT –INFN system

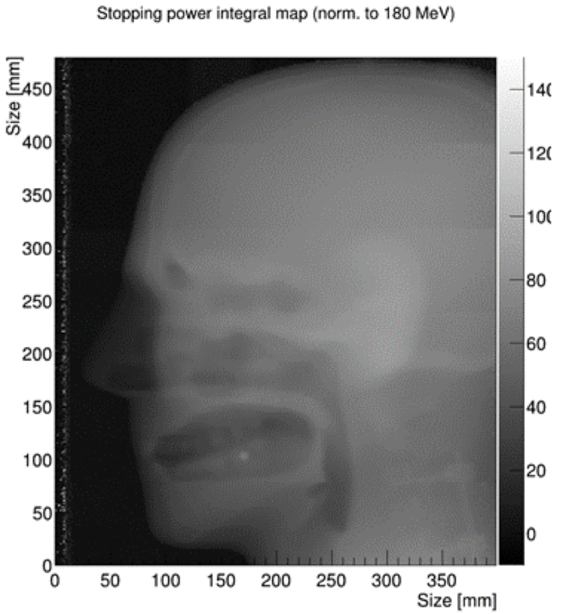
Movie starts from lower jaw ends at upper teeth (5.2 cm range)



X-ray radiography



Tomography region



Proton radiography

Algebraic reconstruction: 64 axial slices;
voxels: 600x600x812μm^3 ~ 0.3mm^3;
400 angles (0.9 deg. uniform spacing)
3.7×10^7 events (selected) .
Total dose ~ 1.5mGy

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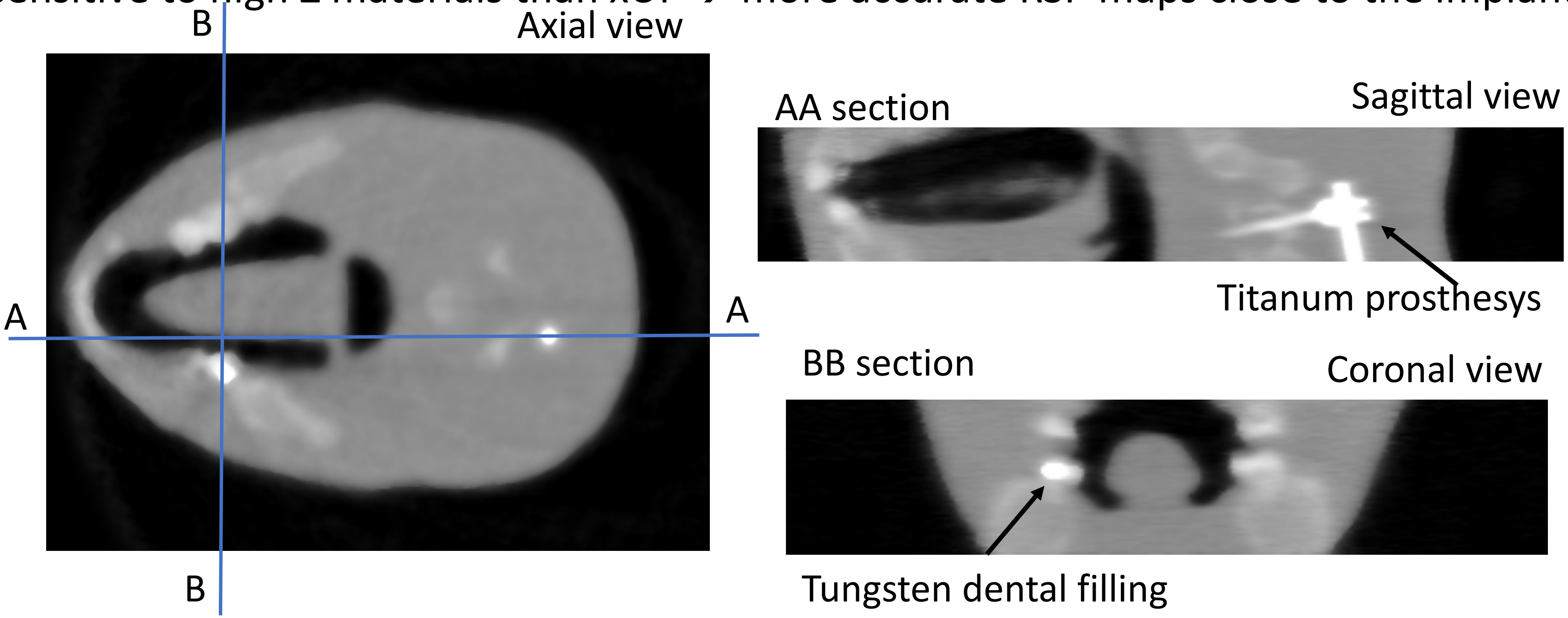
Evidence of reduction of artifacts due to metal prosthesis

- Treatment plans in presence of implanted metal prosthesis difficult because of xCT severe artifacts degrading the RSP maps quality;
- pCT less sensitive to high Z materials than xCT → more accurate RSP maps close to the implants



The grey levels are proportional to the RSP values

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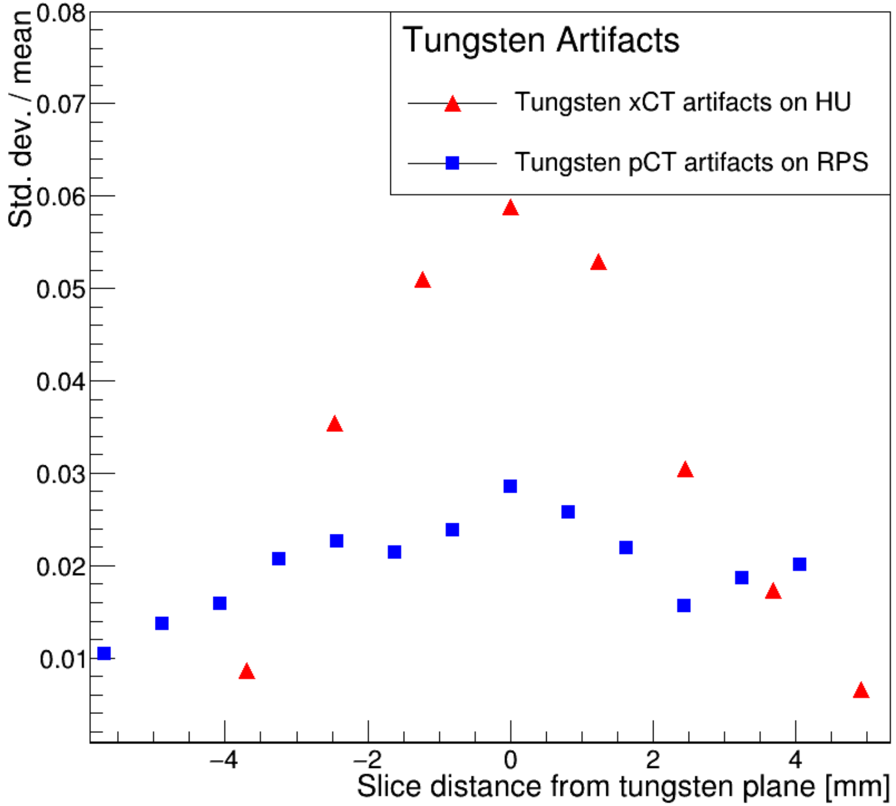
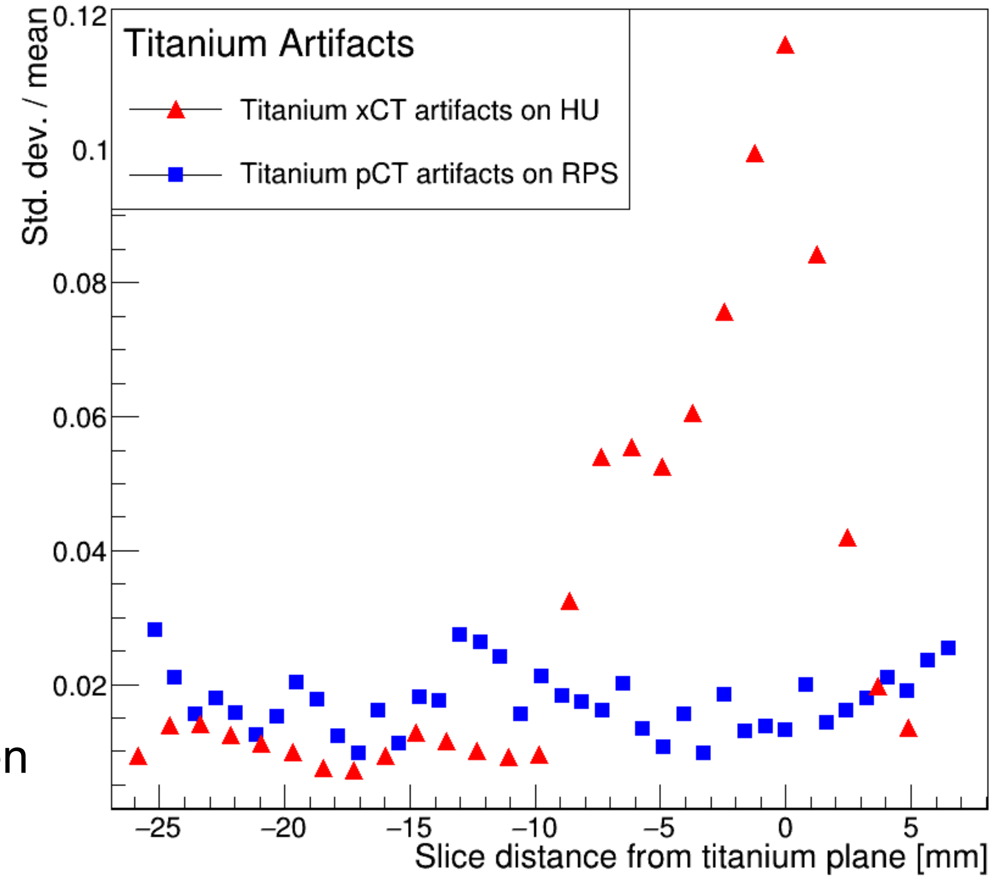
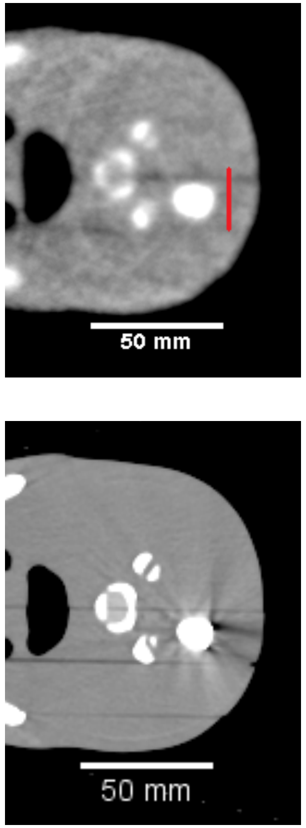
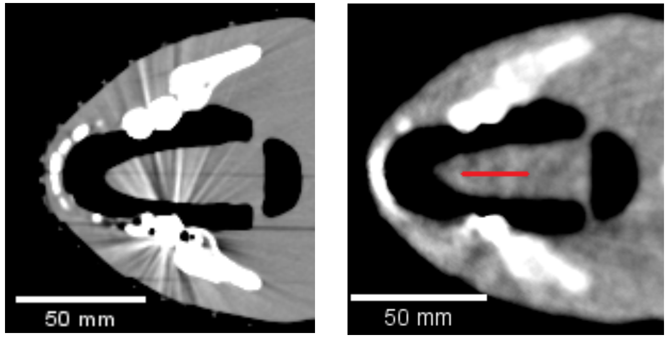
Comparison of RSP and HU standard deviation , calculated within the ROIs close to metal prosthesis







calculated within the ROIs close to the tungsten dental filling



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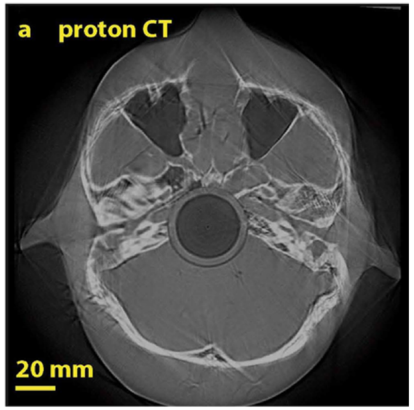
pCT: standard deviations always around 2-3% close to metal

The INFN CSN5 XpCalib Project: A pCT approach to CT calibration for proton treatment planning

- Motivation:
  - Setup and test a new x-CT calibration method for Relative Proton Stopping Power 3D maps determination.
- Objective:
  - Reduced proton range uncertainties in proton therapy.
- Method:
  - Proton computed tomography 3D measurements of a biological phantom
  - New reconstruction algorithm (FBP modified to use MLP) *
  - ≈ 15 min each tomography run (10^8 events 400 angular steps)
- Results:
  - Implementation of the new calibration method in Treatment Planning System and its verification using proton radiographies.

* Simon Rit, George Dedes, Nicolas Freud, David Sarrut, and Jean Michel Létang Filtered backprojection proton CT reconstruction along most likely paths Med. Phys. 40 (3), March 2013

x-CT calibration by pCT

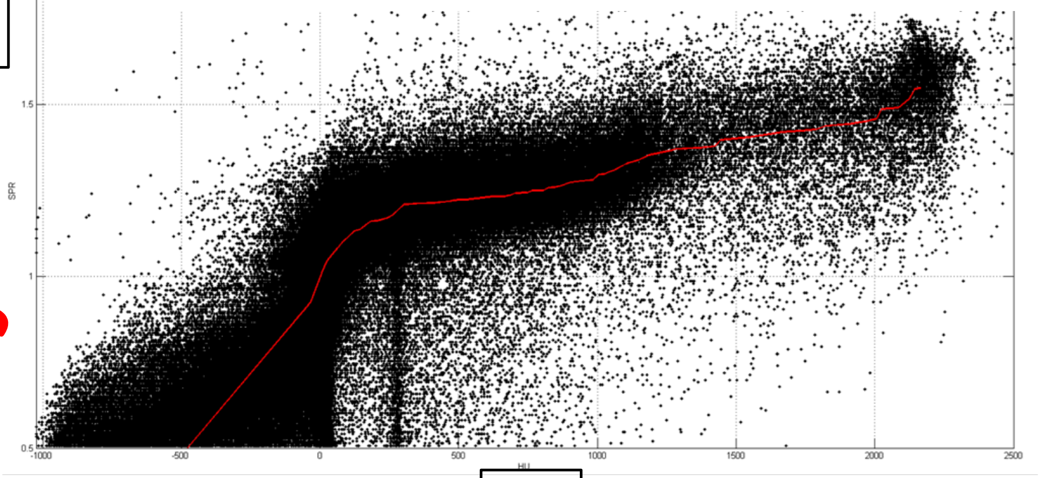


pCT image
(example)

RSP

example

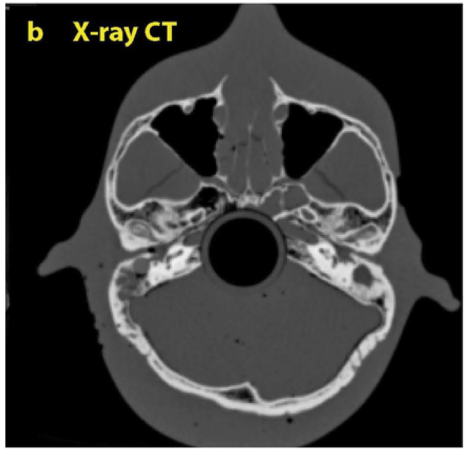
Proton CT SPR vs HU x-ray scatter plot (**example made with plastic phantom head**) Red-line: calibration curve obtained by cross-calibration



HU

Technical Note: CT Calibration for Proton Treatment Planning by Cross-Calibration with Proton CT Data
Paolo Farace *et al.* 2020 *Med. Phys. MEDICAL PHYSICS Volume48 ssue3 1349-1355*

Register the two different images → same reference systems and unit length, deformation correction possible

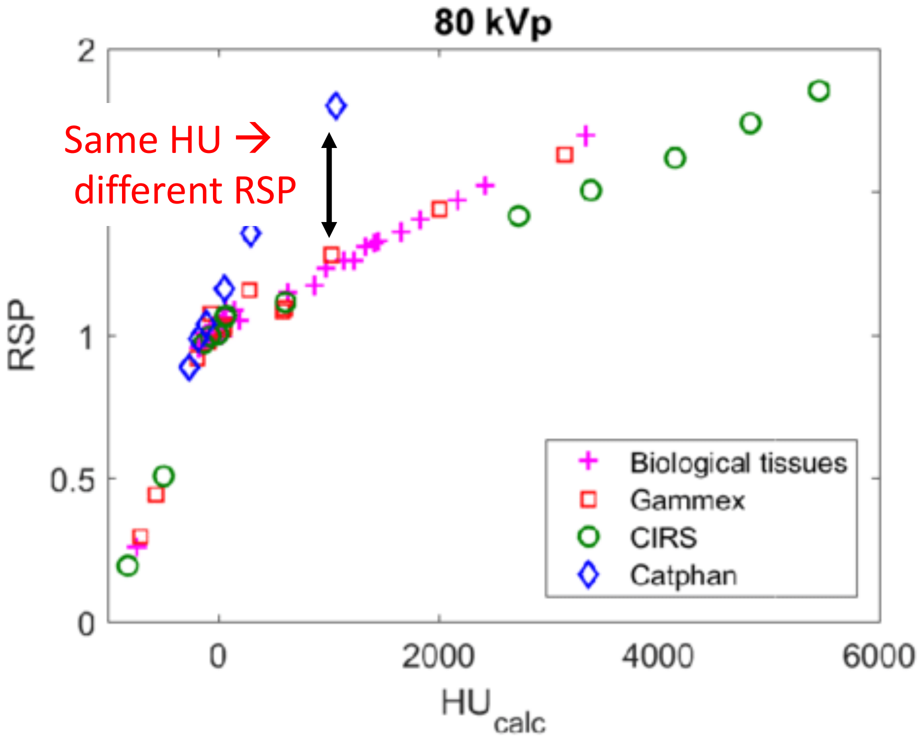


x-CT image

- **Y-axis** directly measuring the RSP by proton Computed Tomography (avoid calculation using mean excitation energies);
- **X-axis** using biological tissues as a reference (avoid tissue substitutes)

Tissue substitute method : Artificial (plastic) materials mimiking the real tissue for what concerns material and electron densities scanned by a x-CT system and their HU measured.

Problem: Plastic Tissue equivalent material compositions differ from real biological tissues in elemental composition



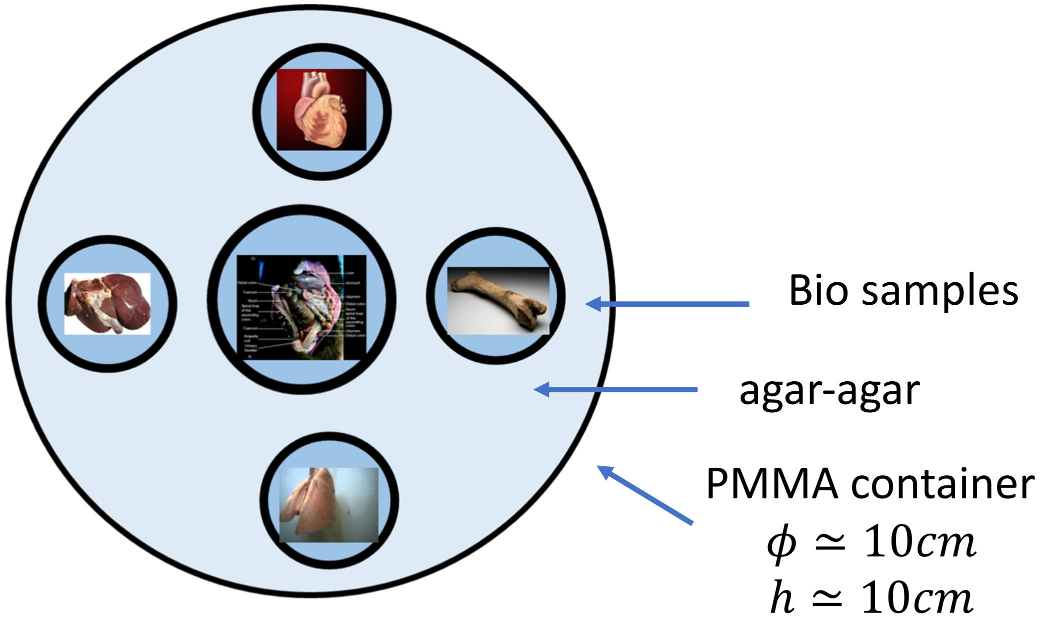
Phys. Med. Biol. 63(23) · Nov. 2018

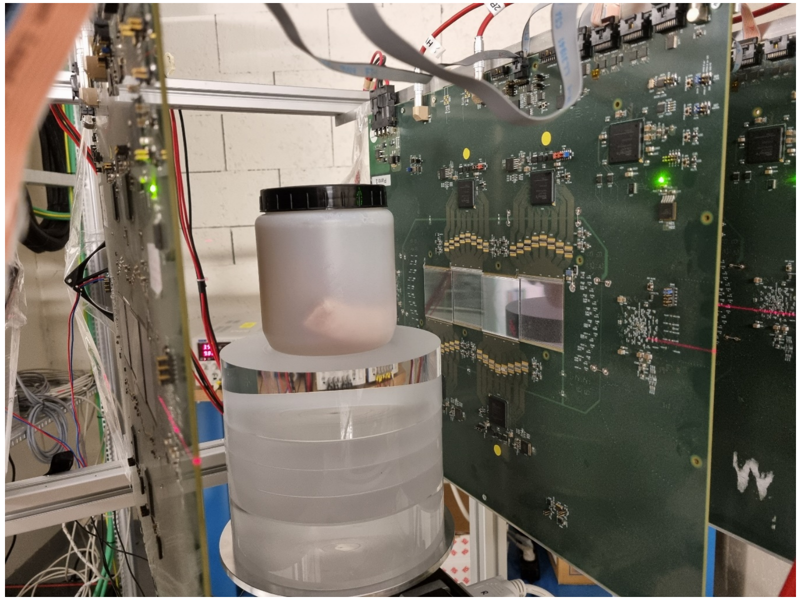
Biological phantom

- To avoid the tissue equivalent material problem we propose to implement a biological phantom

- Animal tissue samples stabilized in formaline, rehydratated and finally suspended in hydrogel.

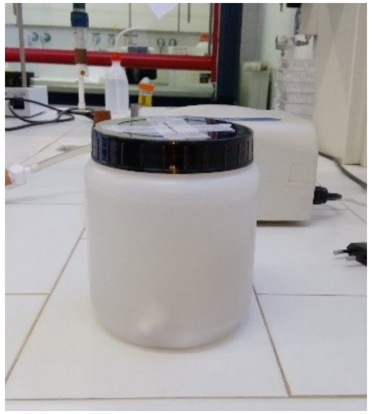
- Samples hosted in a 115 mm diameter container filled with agar-agar.





Calibration of the x-CT with the biological phantom

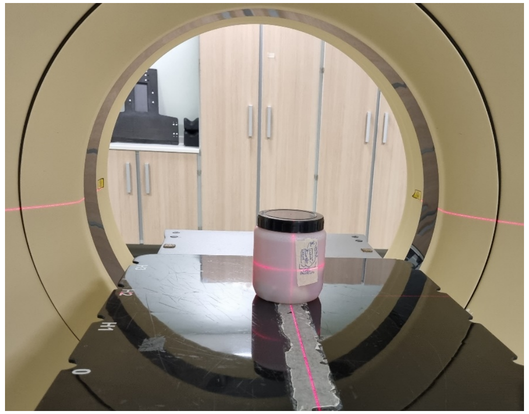
- One phantom imaged by xCT and pCT systems
- HU (from xCT) are '*correlated*' to SPR (from pCT), pixel-wise, to obtain the calibration function:
  - $SPR(x, y, z) = \boldsymbol{f}(HU(x, y, z))$

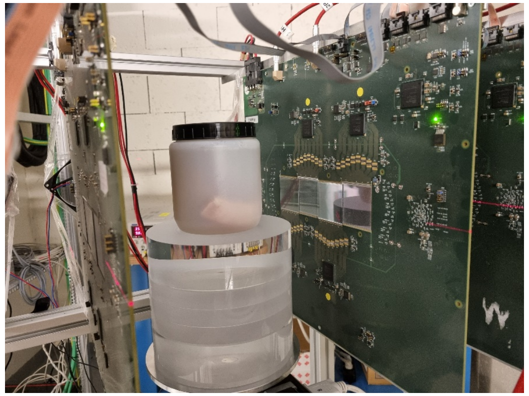


Biological phantom

xCT

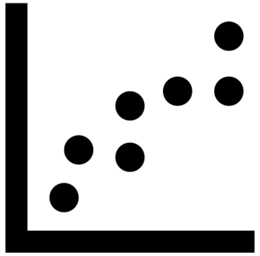
pCT





HU

SPR

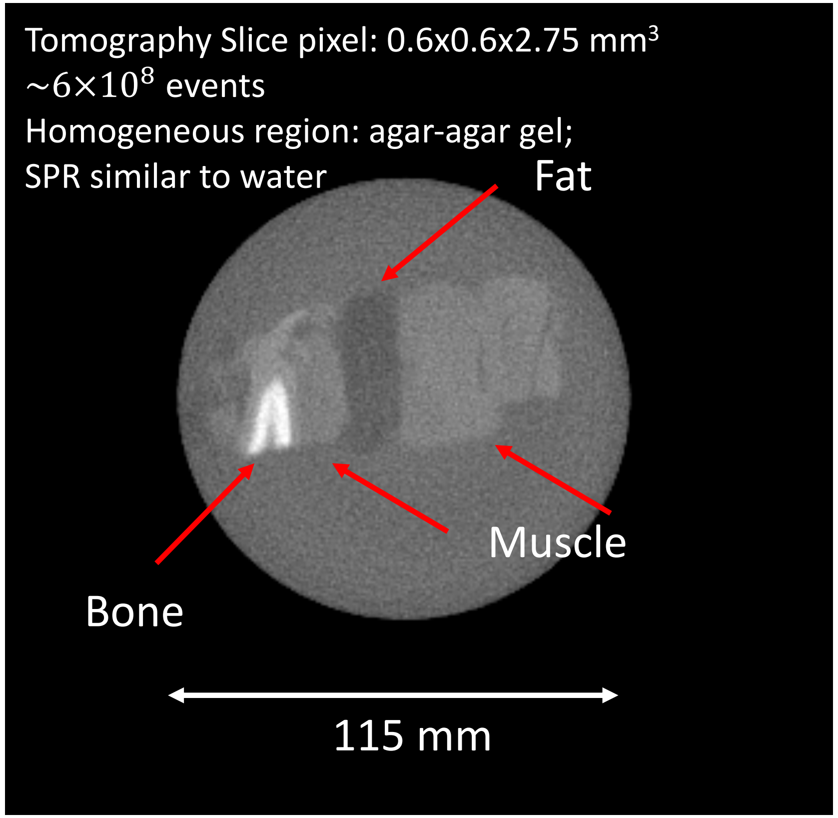


Technical Note: CT Calibration for Proton Treatment Planning by Cross-Calibration with Proton CT Data

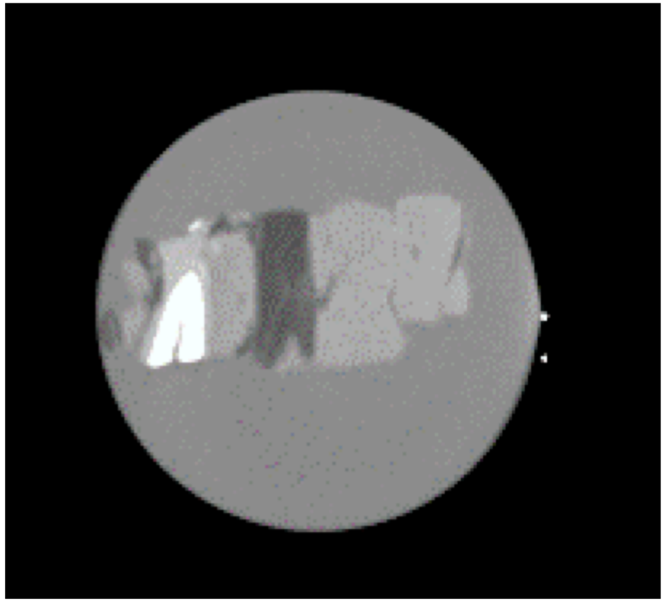
Paolo Farace *et al.* 2020 *Med. Phys.* In press. [https://doi.org/10.1002/mp.14698]

Stabilized bovine phantom pCT

pCT



xCT



X-ray and proton tomographies of the stabilized biological phantom

- ❑ **Now in progress: reconstruction of the cross-calibration curve - scatter plot**

The consistency test

1. x-CT of a bio-phantom with different materials wrt the one used for calib.
2. Model of bio-phantom importing results of 1) in TPS
   A. Using old calibration
   B. Using new calibration
3. Proton radiography prediction from TPS of bio-phantom in case 2A and 2B
4. Real proton radiography of the bio-phantom
   - Using pCT system
5. Difference of radiographies (measured – predicted)
   - Old calibration
   - New calibration

Perspectives:
XpCalib for other therapy centres

- The x-CT calibration via pCT is easily exportable to other proton therapy centres:
    1. bio-phantom pCT scan @ Trento
    2. bio-phantom x-CT @ remote centre
    3. x-CT back to Florence/Trento
    4. Calibration curve
    5. Shipping bio-phantom back to Trento
    6. Verification radiography at Trento
- No need of new hardware
    - One x-CT image + one pCT image + one radiography

Conclusions

- **Proton computed tomography (pCT): a novel medical imaging modality for mapping the distribution of proton relative stopping power (RSP). Compared to conventional X-CT, it has the potential to provide more accurate RSP measurements.**
- **pCT-INFN apparatus installed since 2018 at Trento proton Therapy Centre experimental line (220 MeV proton beam) for pre-clinical studies.**
- **Tomographies of non-homogeneous phantoms showed RSP values in agreement with expected ones at level of 1% and metal artifacts reduction.**
- **On-going x-CT calibration by pCT using stabilized biological phantoms;**
- **It may be extended to proton therapy centers not equipped with a pCT system.**