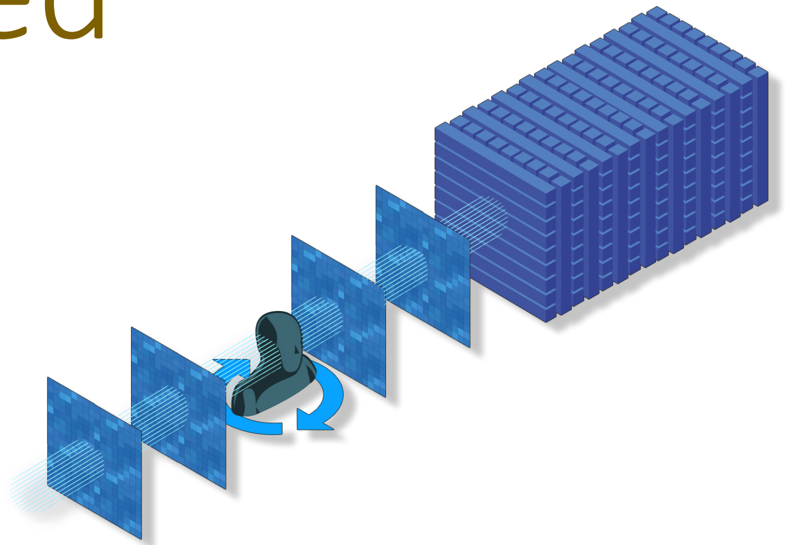
Applications of Particle Physics techniques for proton Computed Tomography



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on behalf of César Jesús-Valls, Thorsten Lux, Tony Price and Federico Sánchez

https://arxiv.org/pdf/2109.03452.pdf

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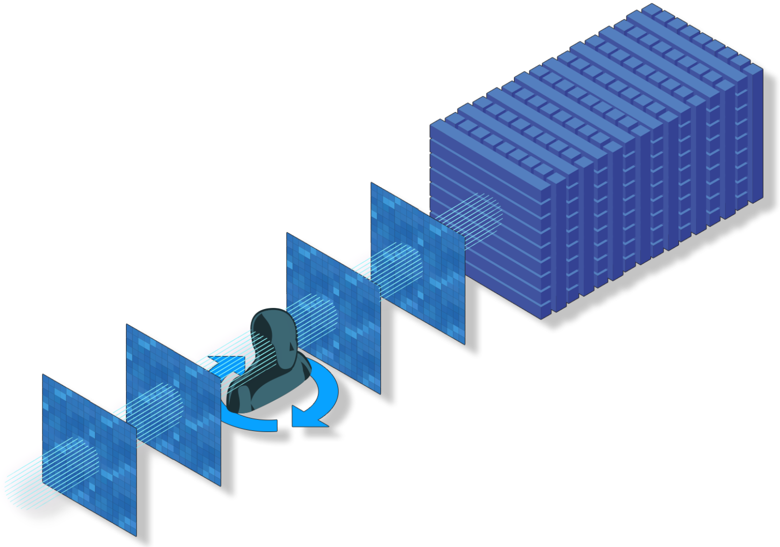
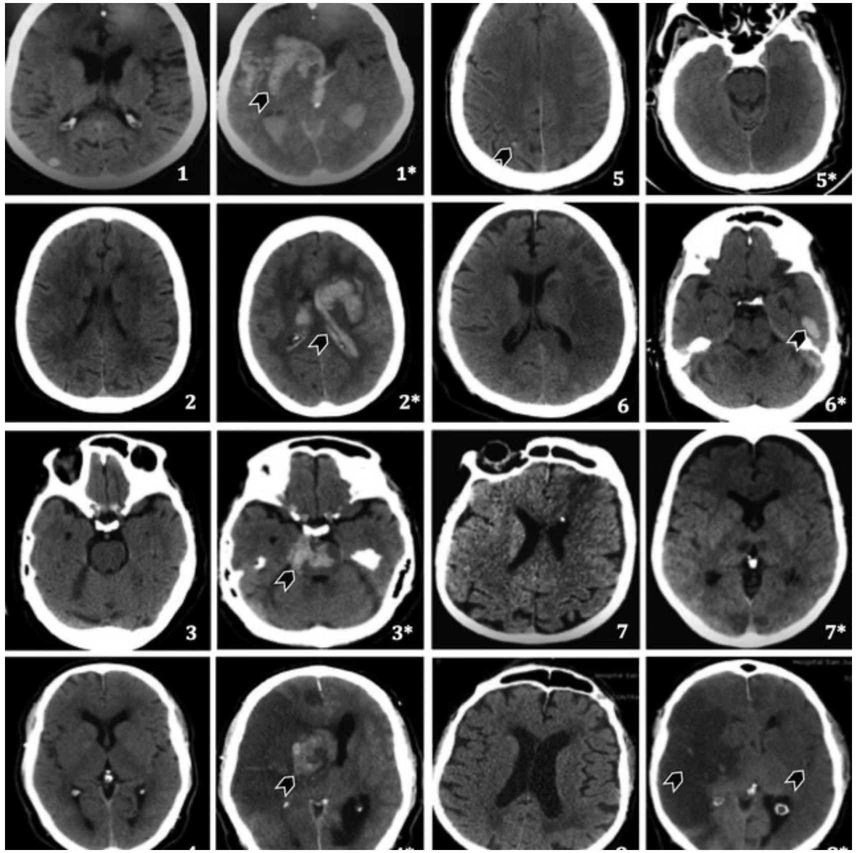
Overview

- Introduction:
  - Computed Tomography
  - Proton radio therapy
  - Protons vs X-rays
  - State of the art on proton CT
  - Novel technologies
- Simulation work:
  - Position tracker
  - Desing and performance of Astra
  - Proton imaging
    - 2D radiographies
    - pCT
- Experimental work:
  - Tracking protons at clinical facilities
  - Testing ASTRA scintillating bars
- Conclusion



Computed Tomography



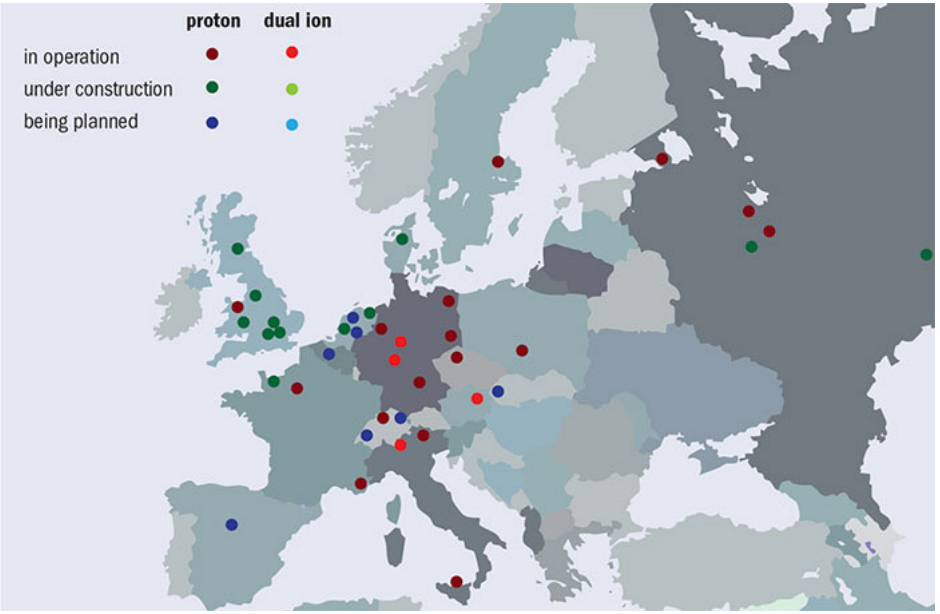
Computed tomography is a technique based on the combination of 2D images or scans taken from different angles around a body (phantom). These images are processed in order to obtain a full 3D view with cross–sectional slices with information through the whole body.

Proton radio therapy

- Treat the tumour with a proton beam
- Proton Radio Therapy (PRT) first proposed in 1946 by Robert Wilson
- First proton therapy treatment was in 1954 at Berkeley Radiation Laboratory
- The world's first proton therapy treatment in a hospital occurred at the Clatterbridge Cancer Centre in 1989

Proton radio therapy

- Rapidly growing and evolving field due to benefits to head and neck cancers and in paediatrics.
- There are currently over **89 proton therapy** sites operational worldwide with a **41 more planned**
- Considerable developments in the UK and Spain over recent years
  - In the UK 2 proton therapy centres Manchester and London
  - 2 centres in Madrid and 10 more to be build in Spain in the following years.
- By the end of 2021, over **170,000** had received proton radiotherapy worldwide



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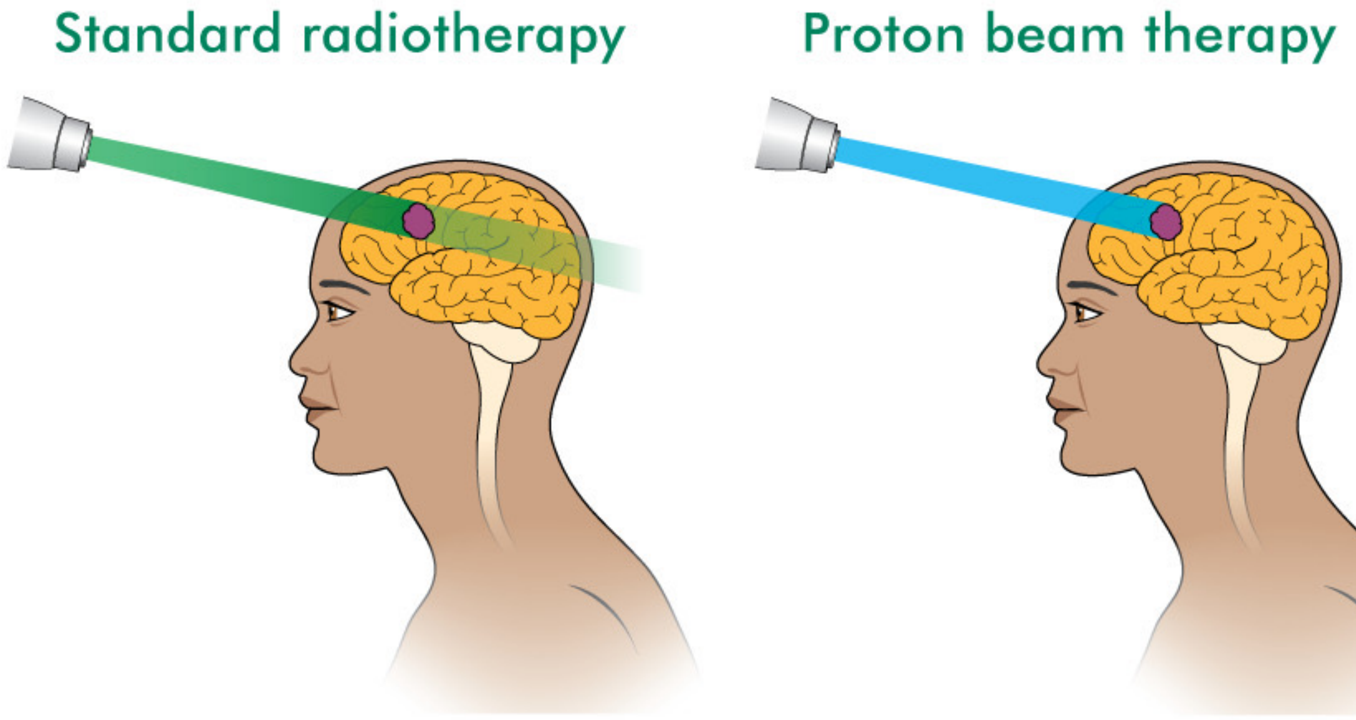
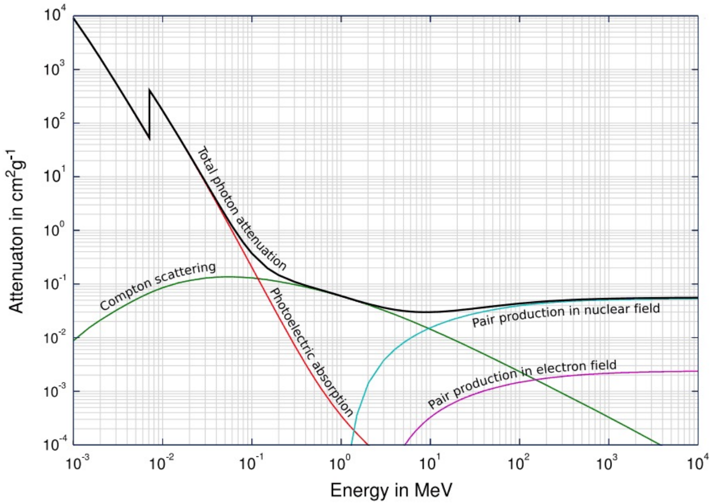
Proton vs X-rays

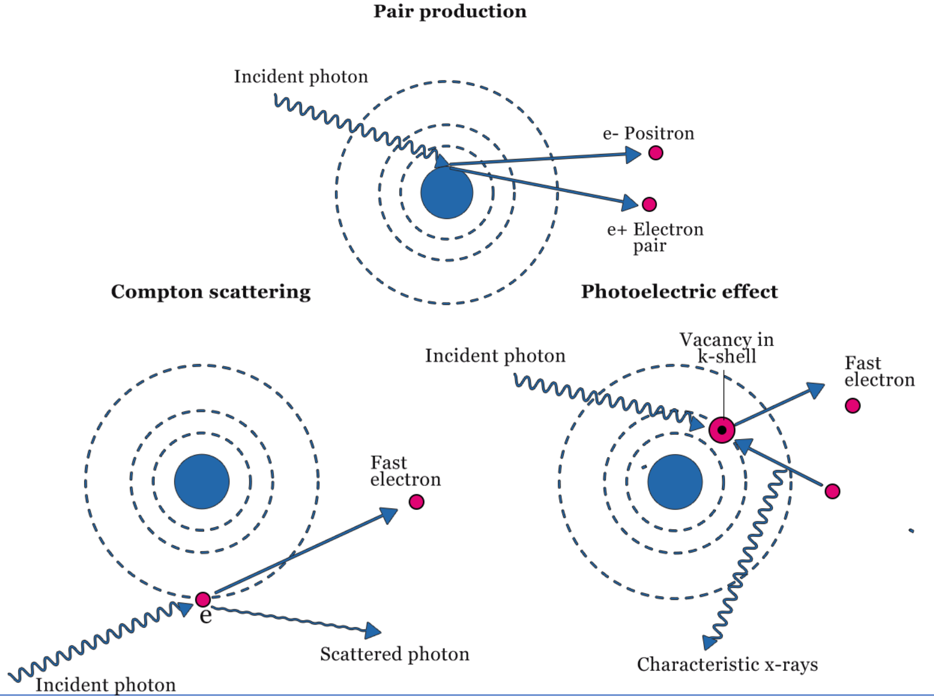


The differences with how protons and x-rays interact with matter affect dramatically the treatment's toxicity

Photon interactions

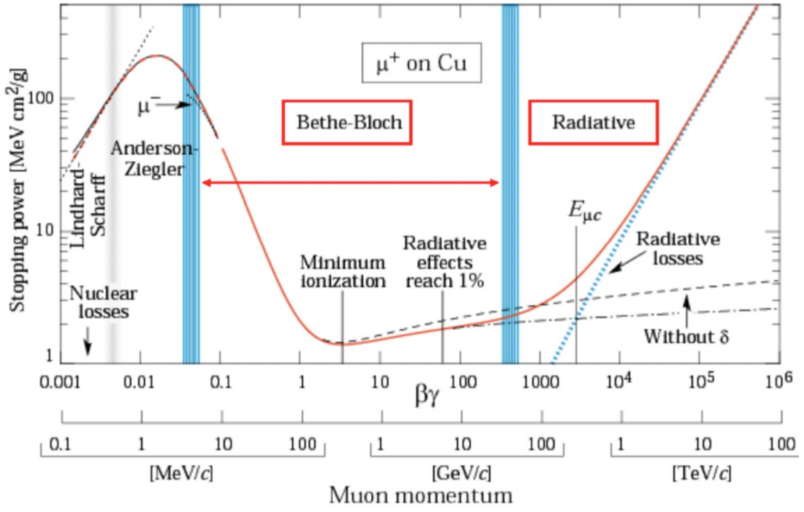
- **Pair production:** Electron-positron pair is generated and thus the energy of the photon has to be above 1.02 MeV (2 $m_e c^2$).
- **Photoelectric absorption:** Interaction between an inner electron strongly bounded to the atom and a photon, typically x-ray. The rate of this interaction depends on the atomic number as Z^{4-5} .
- **Compton scattering:** Interaction between an external shell electron, weakly bonded to the atom and a photon. This interaction rate depends linearly on Z.

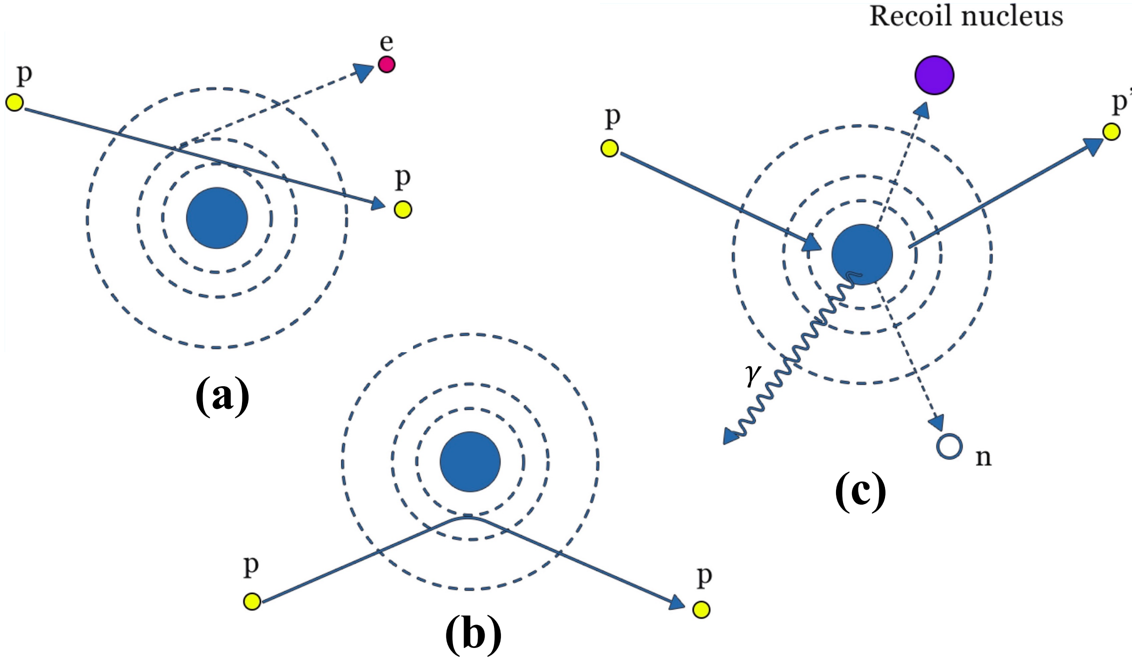




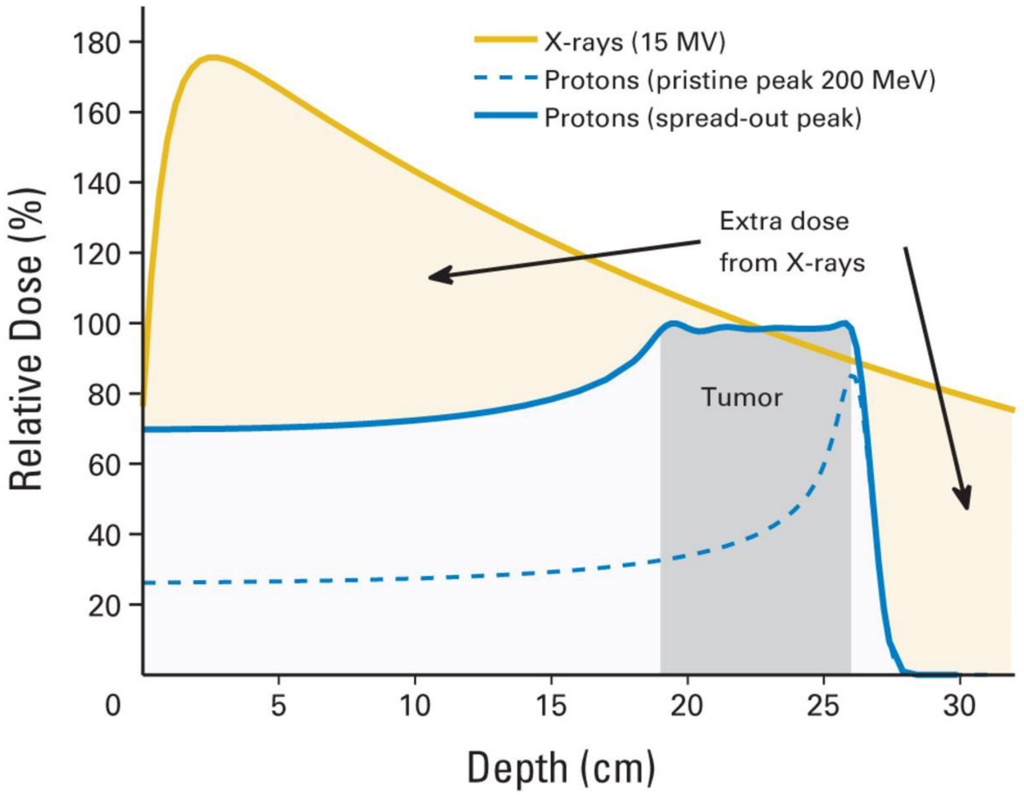
Proton interactions

- Mostly ionisation due to Coulomb interactions:
  - Small deflections
  - Mean free path dependent on energy
- Three main interactions:
  - **a) Inelastic Coulomb interactions:** Ionisation of a shell electron (small deflection)
  - **b) Elastic Coulomb interactions:** Interaction with the nucleolus (large scattering)
  - **c) Nuclear interactions:**
    - Deposit energy far from the interaction point
    - Increase treatment toxicity
    - Cause beam attenuation

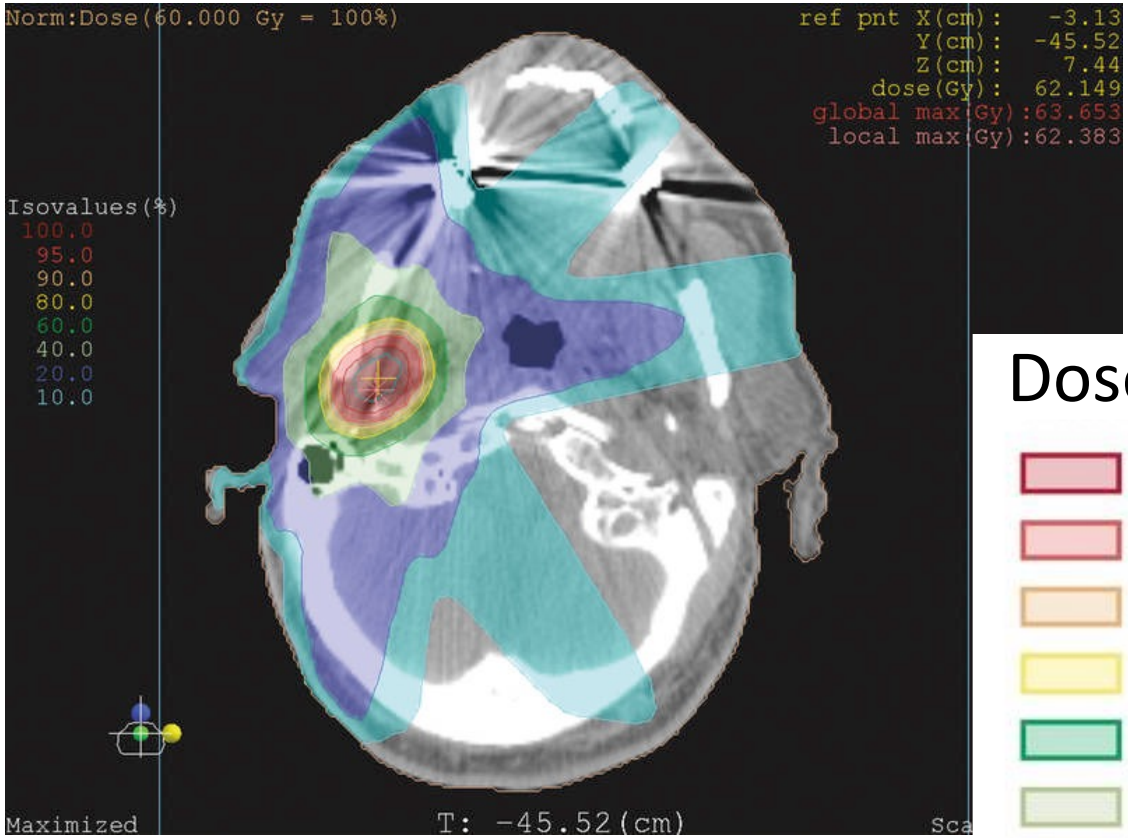




Proton vs X-rays on treatment



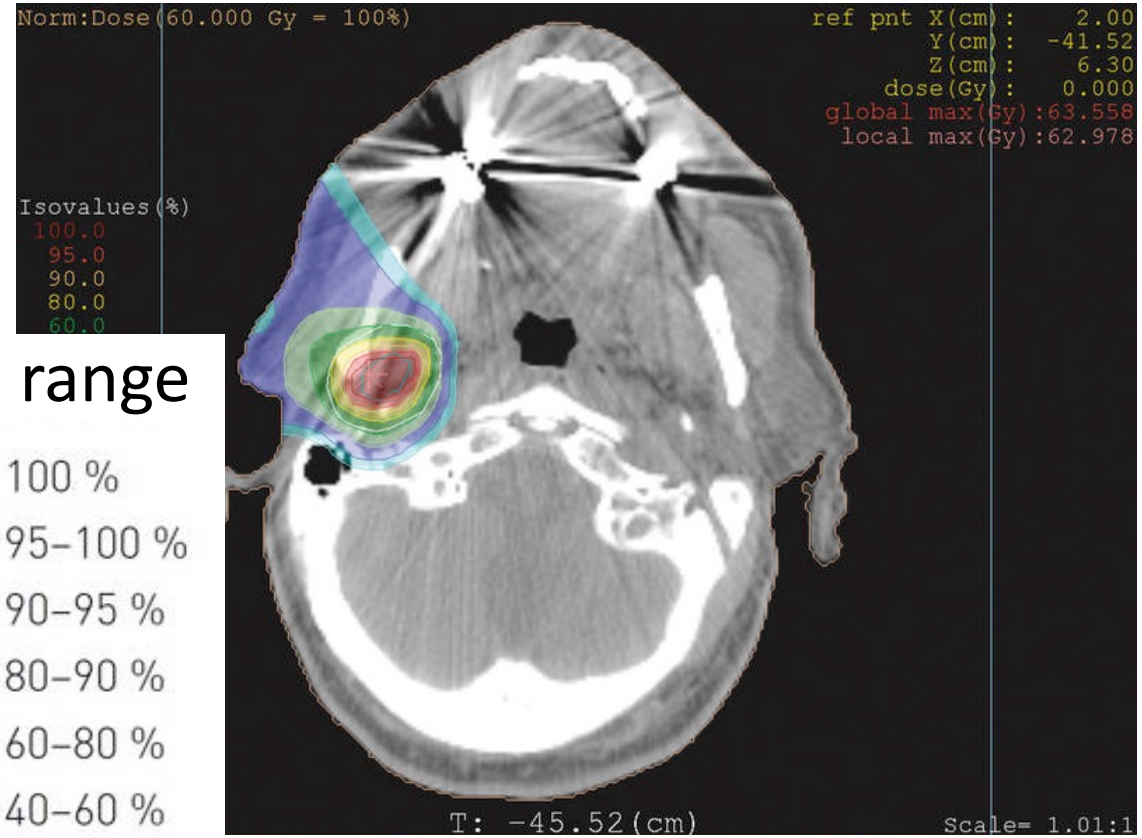
- A beam of photons will deposit energy all along its path following an exponential law
- A proton will lose energy via the Bethe-Bloch formula and as such exhibit a Bragg Peak (BP)
- Most of the energy is deposited just before a proton stops
- Range of charge particle and therefore position of BP set by initial particle energy and materials to be traversed
- No dose deposited after the BP
- Lower dose to healthy tissue reduces the risk of complications in later life and allows for treatment of cancers close to critical organs



X-ray radiotherapy

Dose range

- 100 %
- 95–100 %
- 90–95 %
- 80–90 %
- 60–80 %
- 40–60 %
- 20–40 %
- 10–20 %



Proton radiotherapy

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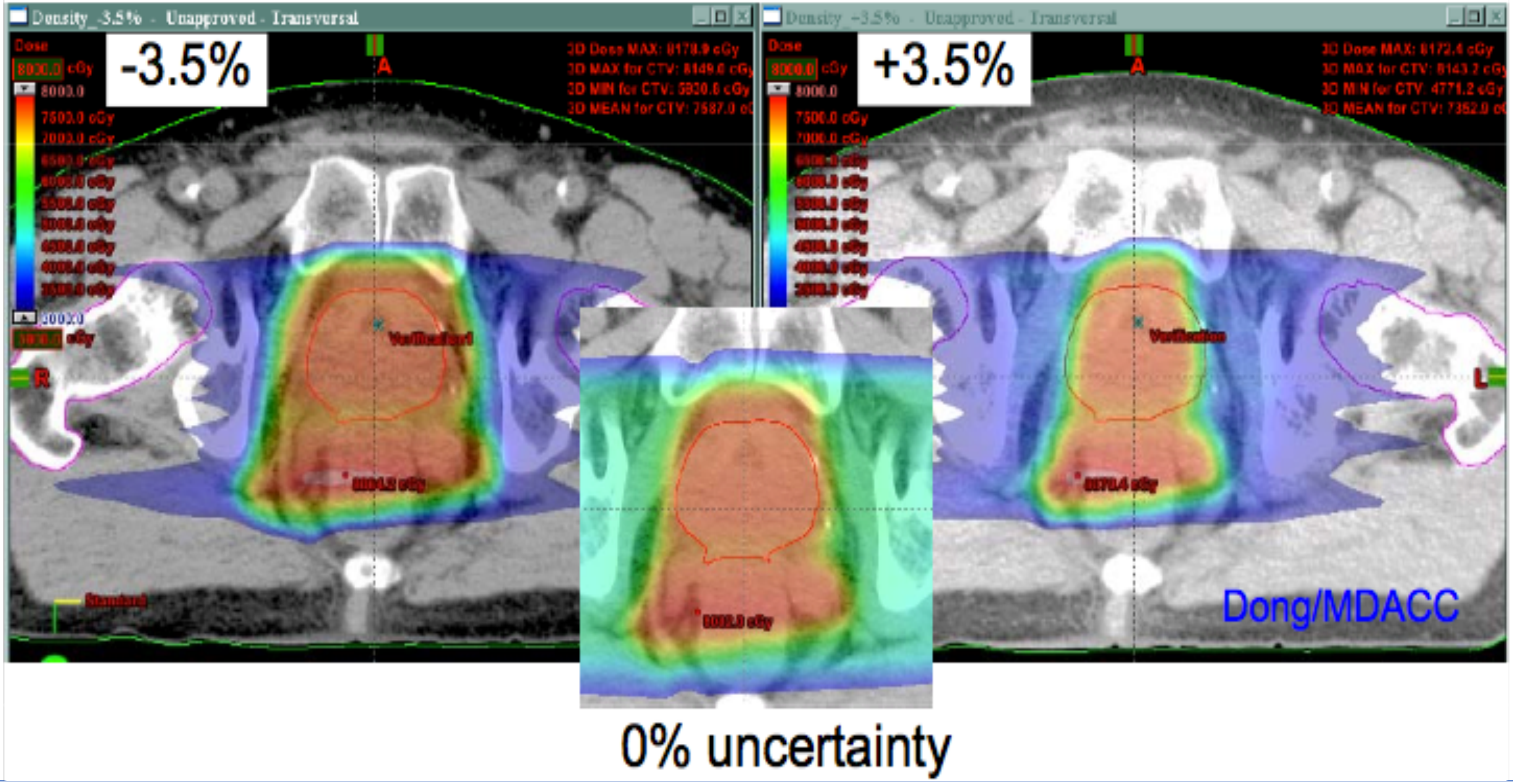
Imaging with x-rays

- Bragg peak: **With great power comes great responsibility**
- Very localised dose deposition needs from very low uncertainty in range (energy).
- So far, stopping power and ionisation potentials of materials are extracted from a conventional x-ray CT scan –> BIG uncertainties!
- Imaging with x-rays, but treating with protons!

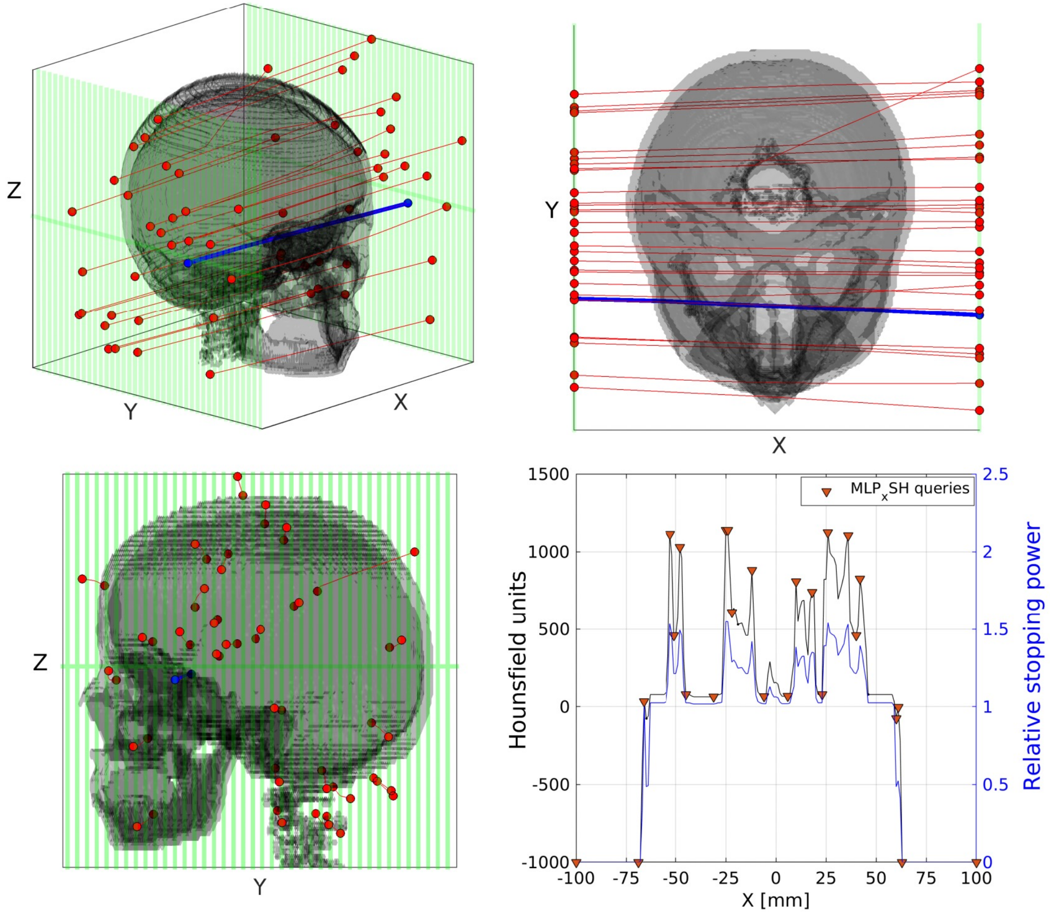
	Uncertainties in SPR estimation (1σ)		
Uncertainty source	Lung (%)	Soft (%)	Bone (%)
Uncertainties in patient CT imaging	3.3	0.6	1.5
Uncertainties in the parameterized stoichiometric formula to calculate theoretical CT numbers	3.8	0.8	0.5
Uncertainties due to deviation of actual human body tissue from ICRU standard tissue	0.2	1.2	1.6
Uncertainties in mean excitation energies	0.2	0.2	0.6
Uncertainties due to energy dependence of SPR not accounted by dose algorithm	0.2	0.2	0.4
Total (root-sum-square)	5.0	1.6	2.4

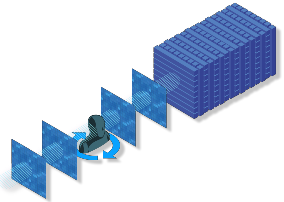
Consequences of big uncertainties



Resolutions needed

- A technique able to measure directly the Proton Stopping Power or the Relative (to water) Stopping Power **RSP**
- When treating with protons, image with protons → **pCT**
- Range or energy resolution below 1%
- Position resolution (voxel size) of ≤ 1 mm



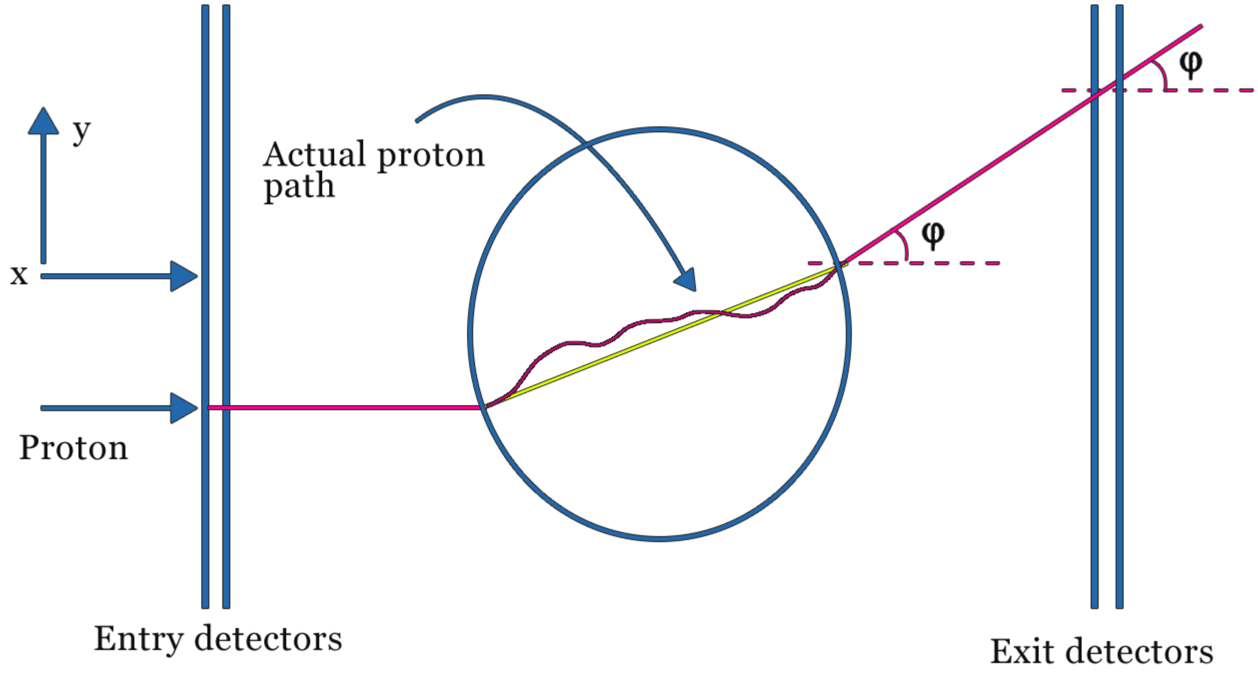


Needs for proton CT

In order to obtain a proton Computed Tomography (pCT) one needs to know:

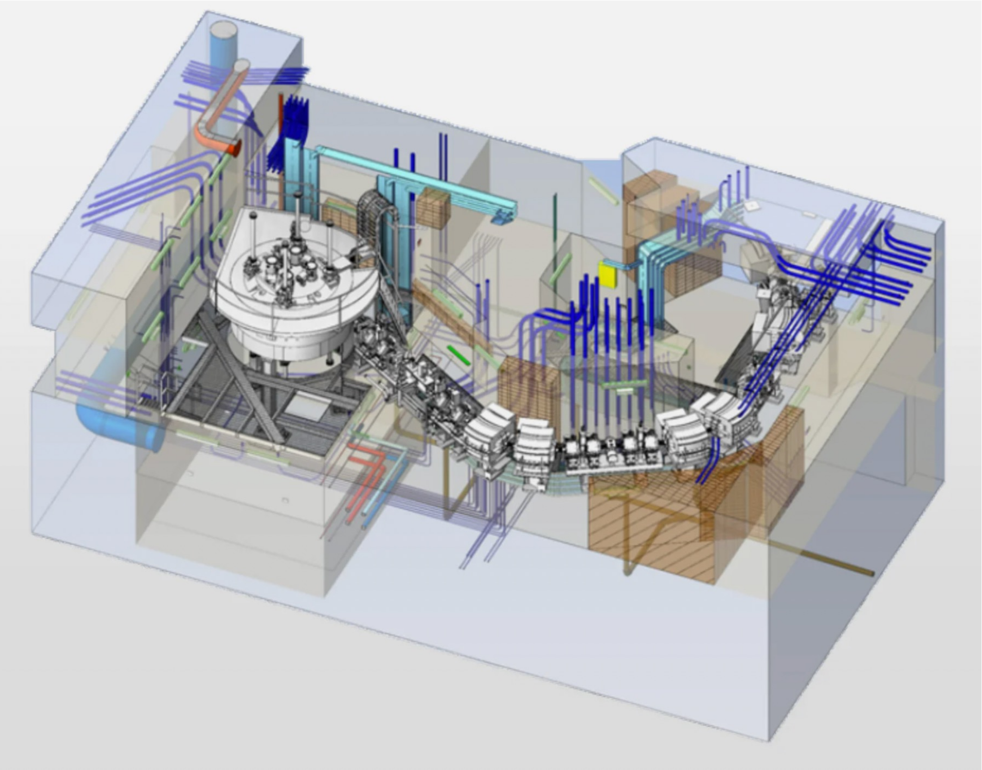
- The protons' entering and exiting points of the imaged body.
- The residual energy after trespassing the phantom.
- How to reconstruct the path within the patient/phantom.

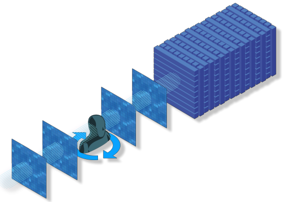
Note: For this work, a Most Likely Path (MLP) algorithm written for the PRaVDA collaboration was used. This algorithm requires from energy measurements.



State of the art on pCT

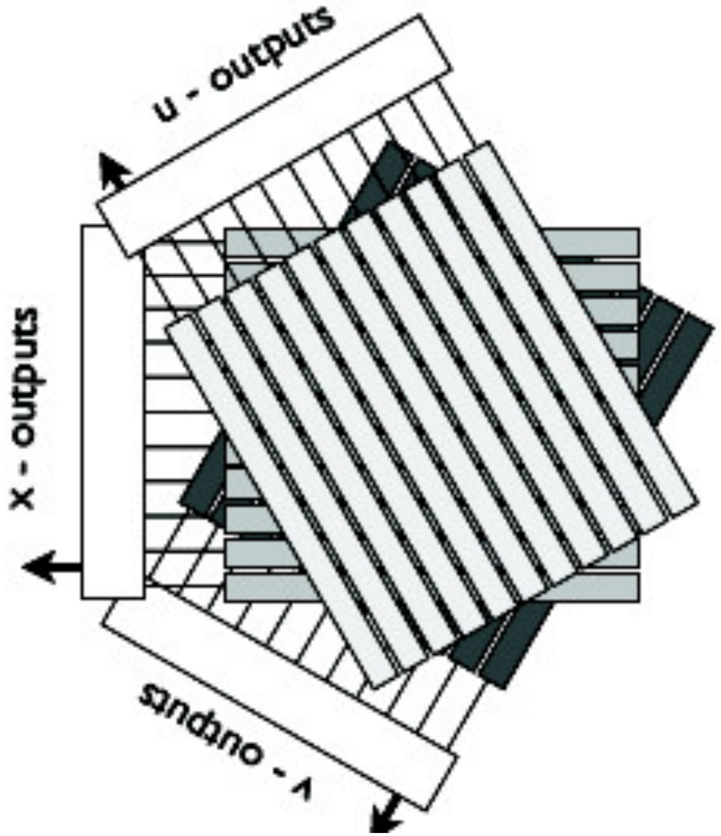
- Clinical beam using energies up to 250 MeV
- The currents provided by the clinical beams during treatment are of the order of 10^9 protons/s:
  - These values aim to be reduced for imaging purposes but there are limitations due to the accelerator properties.
  - Beam time is gold so the faster the better.
- Proton bunch density follows a Poisson distribution.
- Pencil beam used for imaging → Gaussian beam with $\sigma \leq 10\ \mathrm{mm}$





State of the art on pCT

- **Position trackers:**
  - Old technologies (30 years old). Strips sensors (**1D resolution!**) are used in order to track the protons before and after trespassing the phantom.
  - Hybrid sensors with large budget material.
  - Big modules with larger amounts of data.
  - Hard to decouple ambiguities.

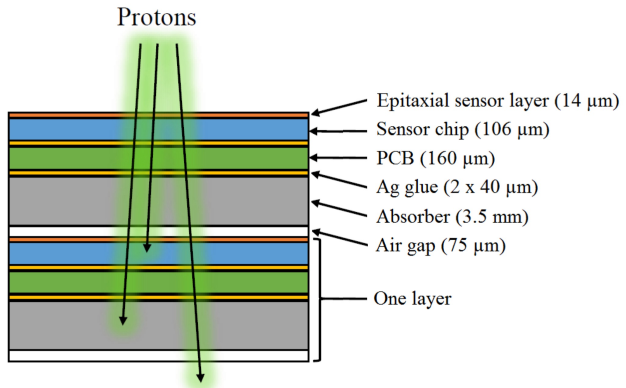


PRaVDA tracking module

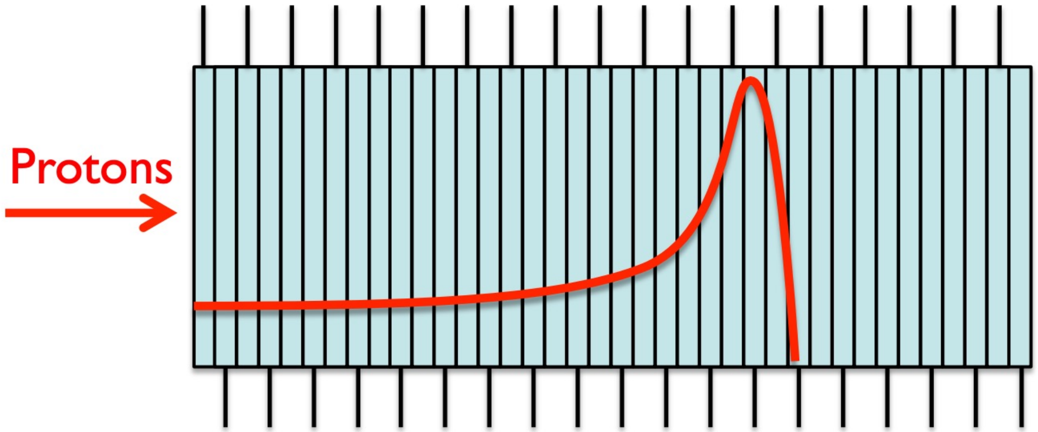
State of the art on pCT

- **Energy tagging:**
  - New technologies under development example
    - **ALPIDE** based calorimeters.
      - Expensive (silicon)
      - **Slow sampling rate** few micro seconds.
    - The plastic scintillator design from **Loma Linda** or the **SUPER-NEMO** based range telescope.
      - Layers of plastic scintillator
      - **Not capable to deal with multi protons**
      - Unable to deal with “kinks”

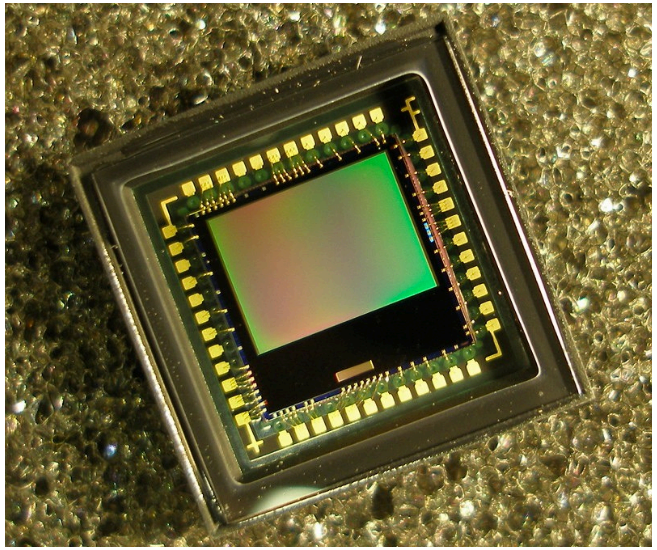
ALPIDE based module



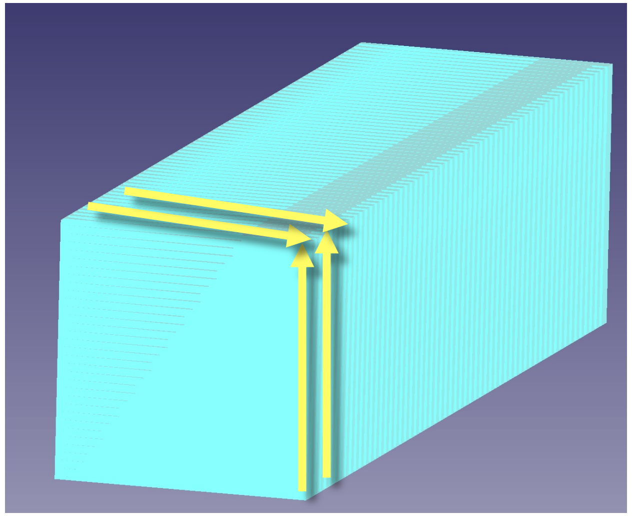
SUPER-NEMO based RT



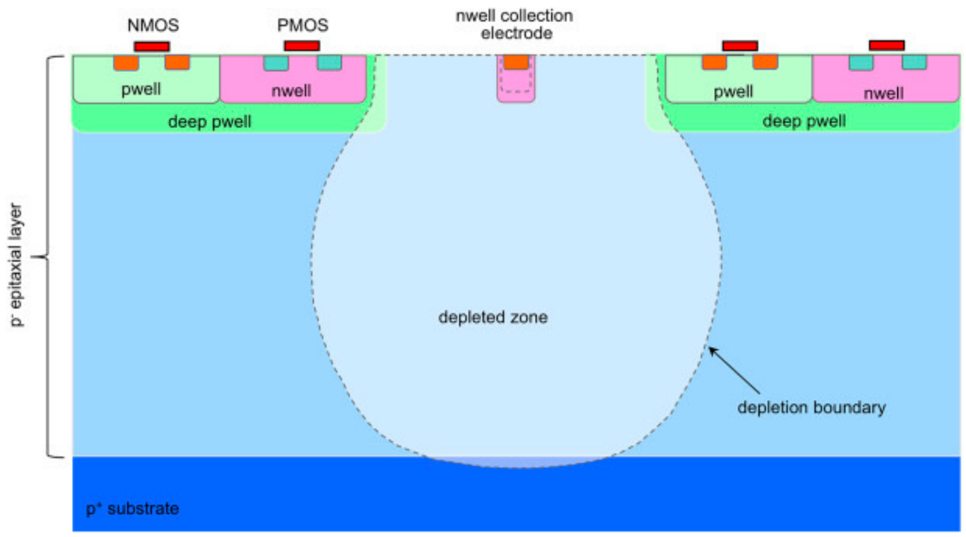
New technologies



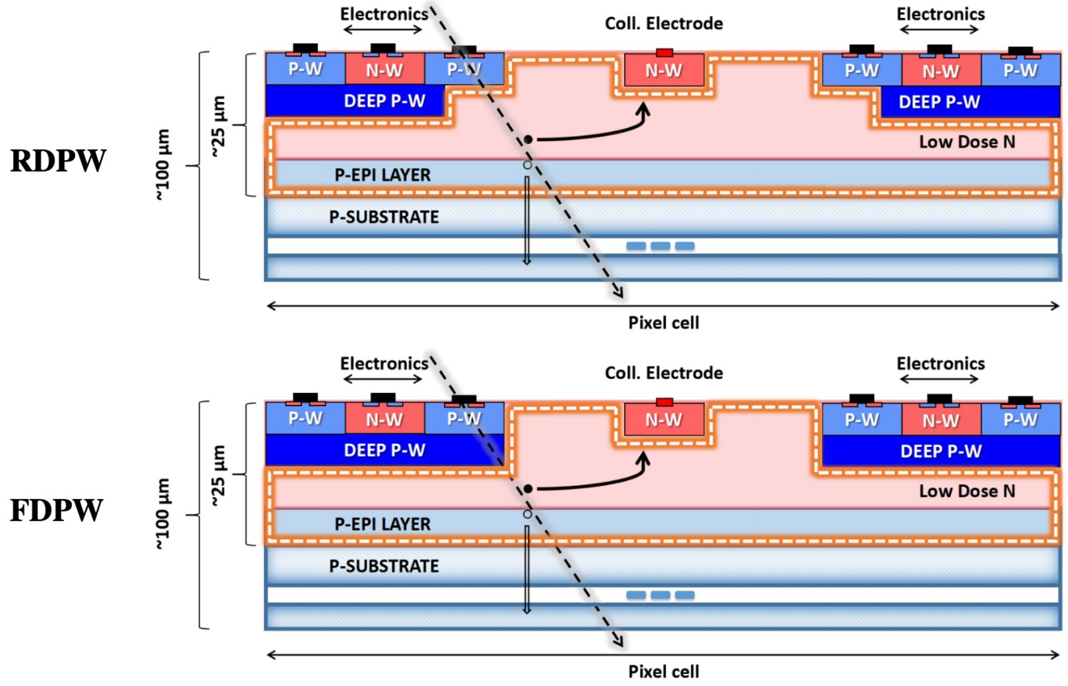
- Depleated Active Pixel Sensors (DMAPS) are a modification of MAPS but faster and able to cope with radioactive environments.
    - Same tech you have in your phone, but cooler.
- **A S**uper **T**hin plastic **RA**nge telescope:
    - Fine segmentation achieving 1D resolution to be able to track individual protons.
    - ASTRA module segmented in bars oriented in perpendicular directions to the beam.



MAPS and DMAPS



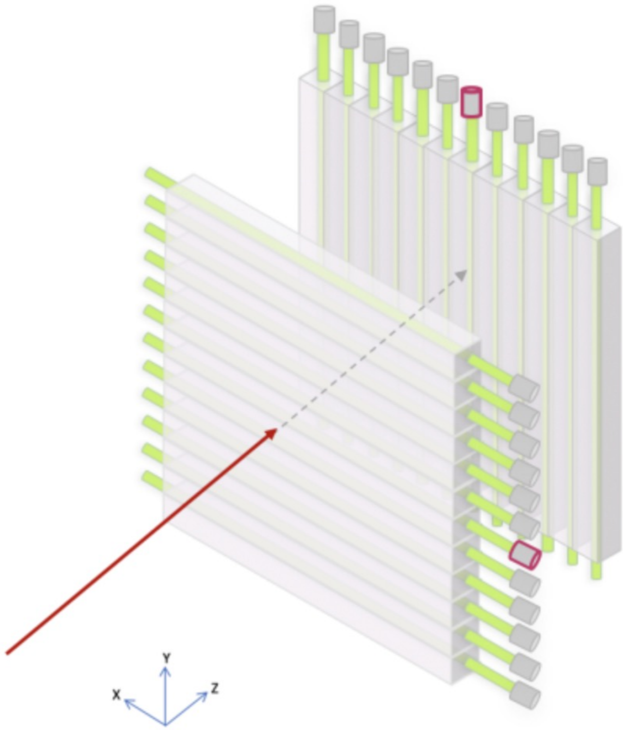
Sketch of a transverse of an Active Pixel Sensor structure showing the depleted boundary.



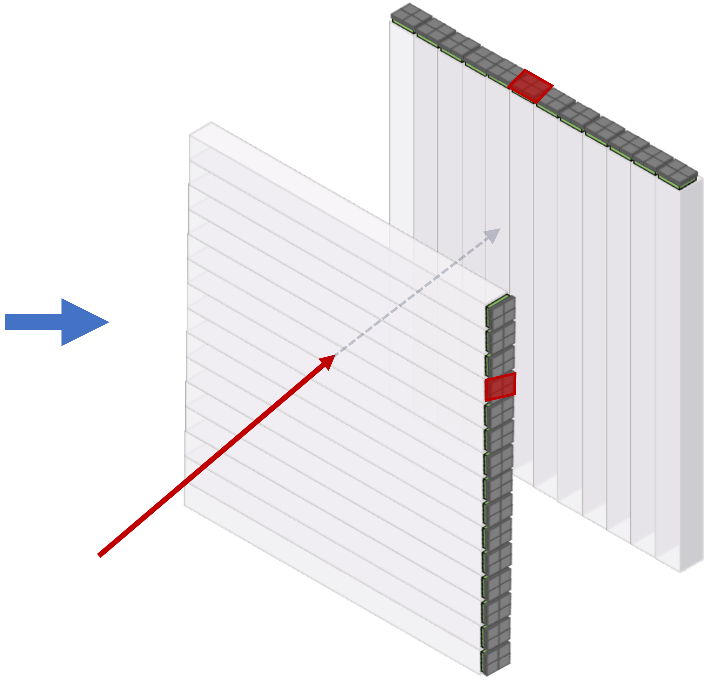
Sketch of the structure of the TJ-monopix (DMAPS) chip with a partially Removed Deep P-Well (RDPW) (top) and Full Deep P-Well (FDPW) (bottom) [1]

The idea of ASTRA

Fine **G**ranulated **D**etector



ASTRA



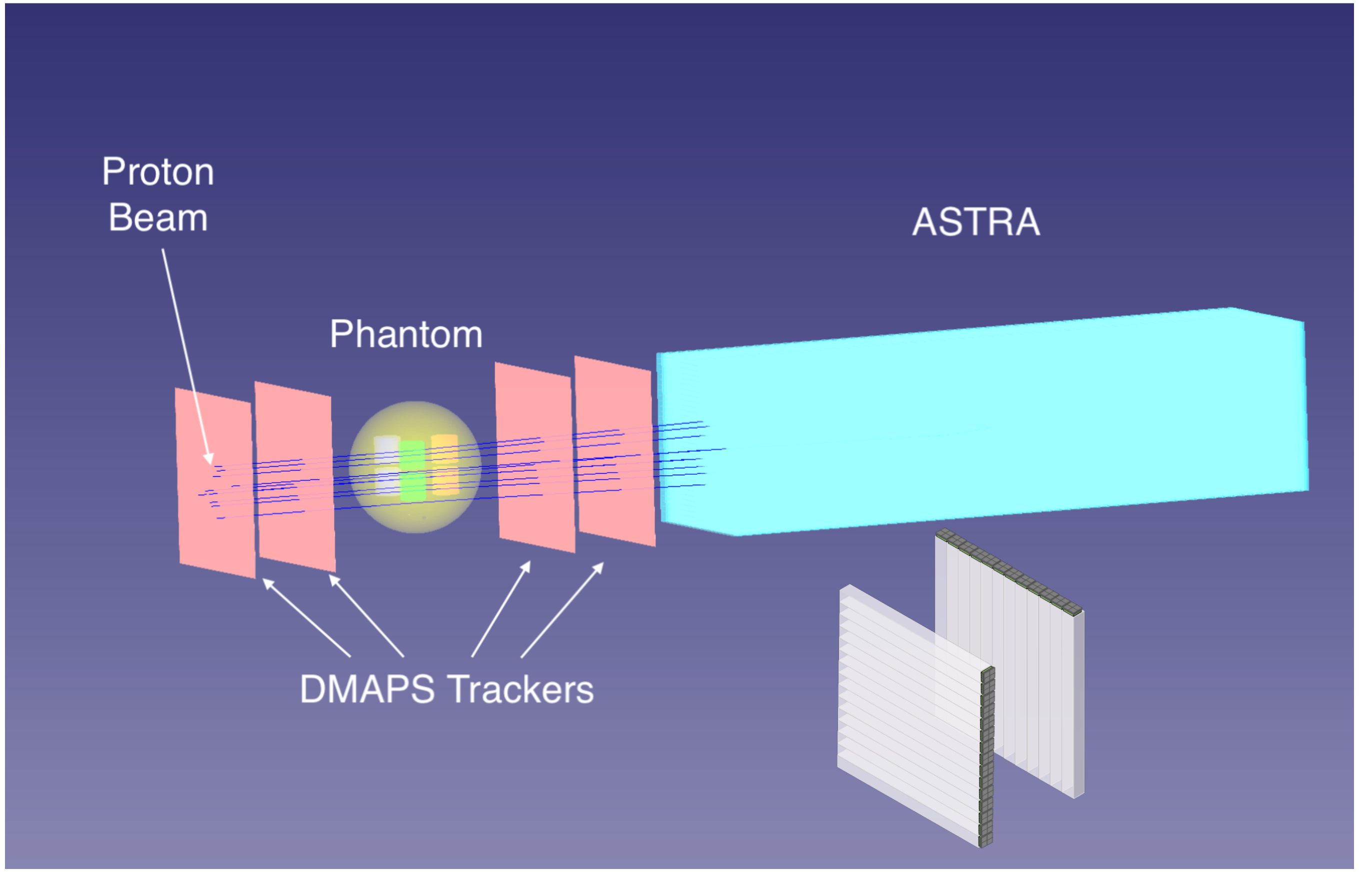
Segmentation in ASTRA allows to actually track protons!

Simulation work for pCT

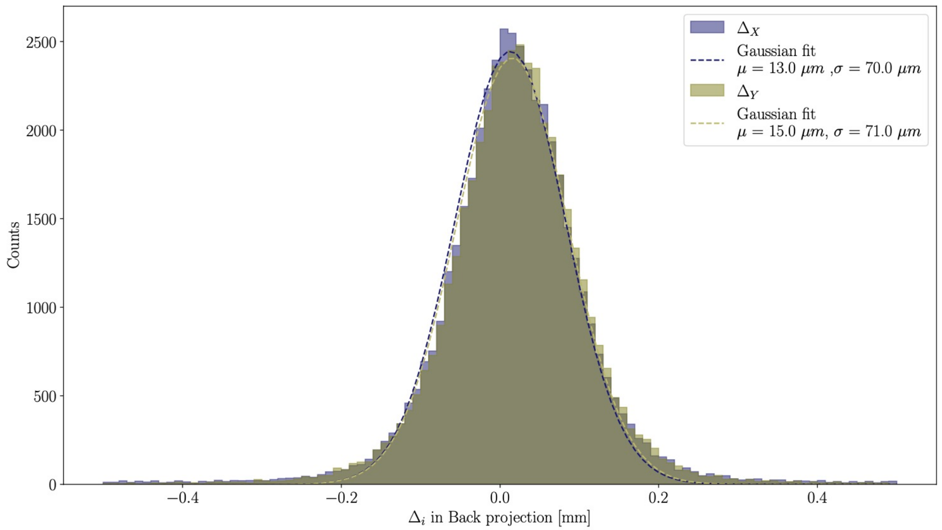
- **Proton tracking:**
  - **DMAPS** [3,4,5] with for the front (2) and back (2) tracking system with pixels of 40x40 μm^2 and a full size of 10x10 cm^2.

- **Energy tagging:**
  - **ASTRA** for the residual energy measurement with 120 layers of 36 bars of 96x3x3 mm^2 inspired on the FGD at T2K [6].

The technologies, presented in [2], simulated with **Geant4/10.06.p03** and the physics package **QGSP_BIC** at the BlueBear computer.



Tracking performance

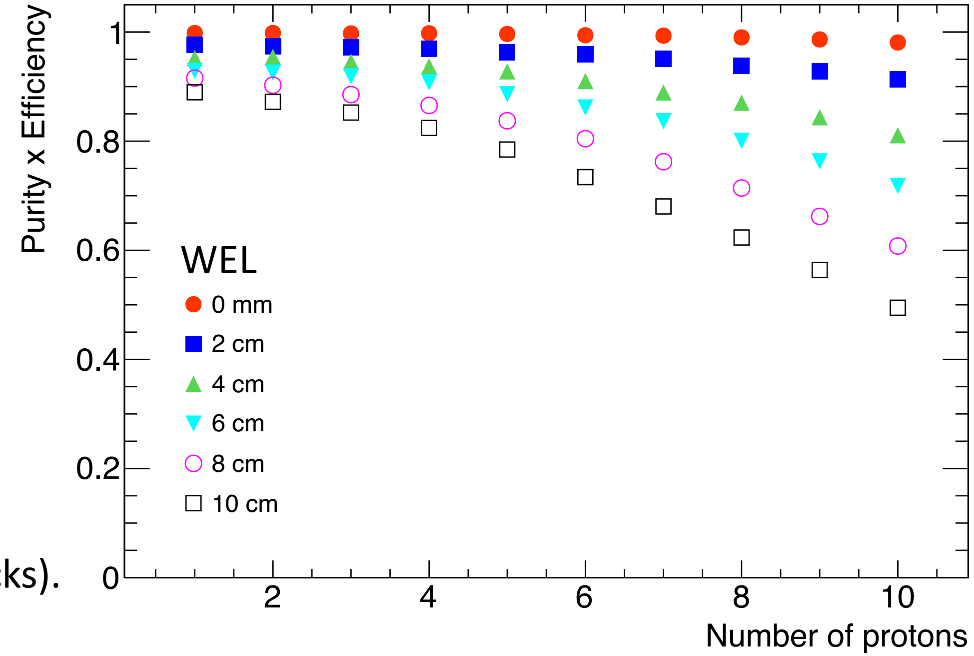


Position resolution on back and forward projections of 70 μm

The figure of merit for the front tracker is $Purity \times Efficiency$ defined as:

$$Purity = \frac{Well\ Reco\ Tracks}{Total\ Reco\ Tracks}$$

$$Efficiency = \frac{Total\ Reco\ Tracks}{Total\ \ Tracks}$$



As function of the number of protons per event for different water equivalent lengths (WEL).

180 MeV protons with a Gaussian beam distribution with $\sigma = 10$ mm.

Note that MCS will affect on the efficiency (lost protons) and purity (crossed tracks).

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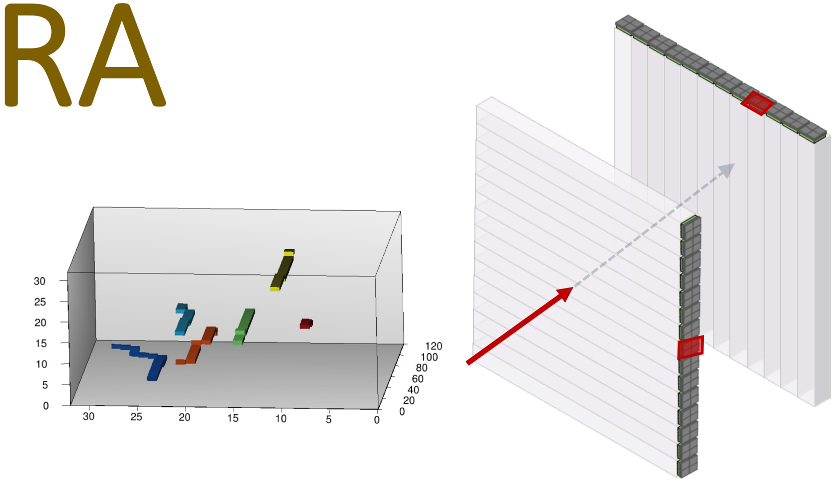
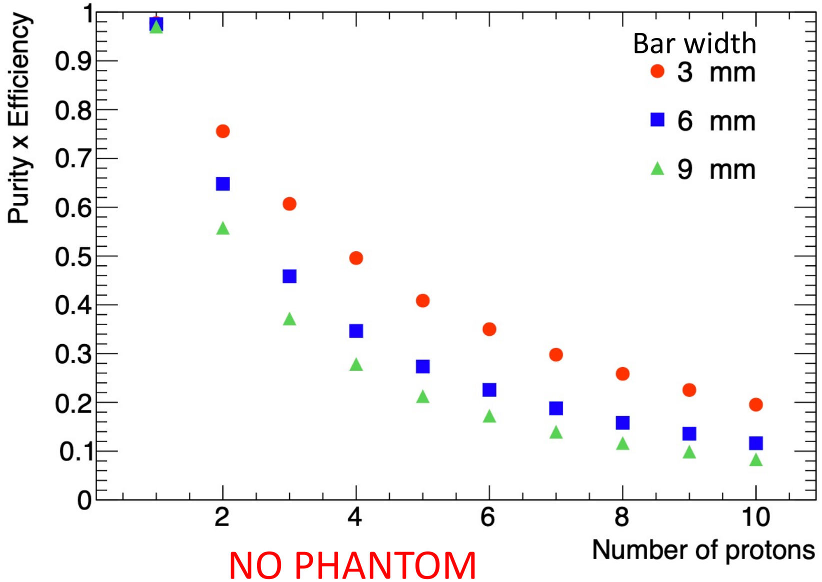
Matching tracks with ASTRA



- Project DMAPS tracks into ASTRA first 2 layers (3D seeding points in ASTRA), connect trajectories that are closer.
- For the seeding points, assume that the track goes forward, look for the next closer 3D point and propagate forward. Hits can not be shared between tracks.
- Different bar sizes where tested trying to study costs and figures of merit such as $Purity \times Efficiency$ and energy resolution.

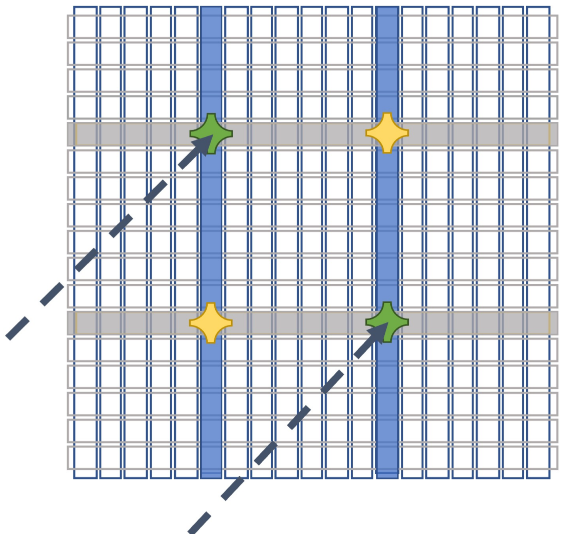
NOTE: The reconstruction can be improved in the future with dedicated work, we only built a minimal version to show the concept.

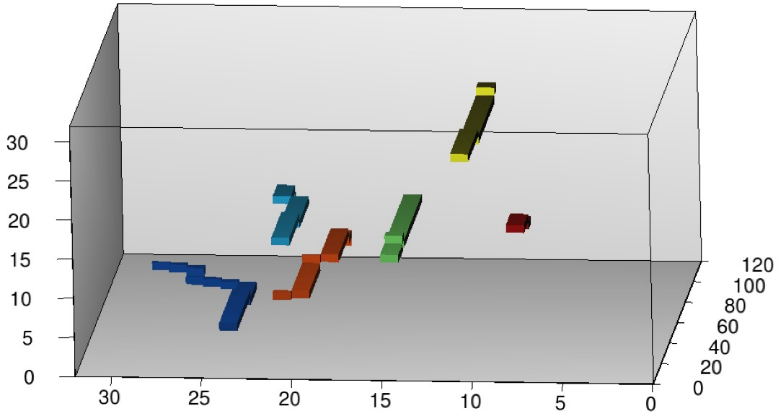


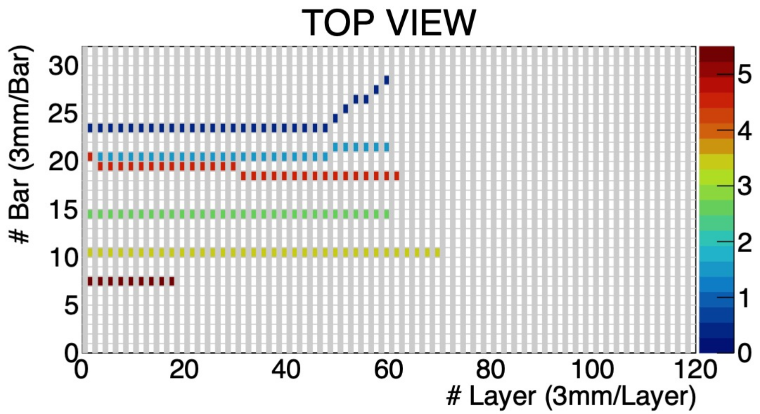
NO PHANTOM

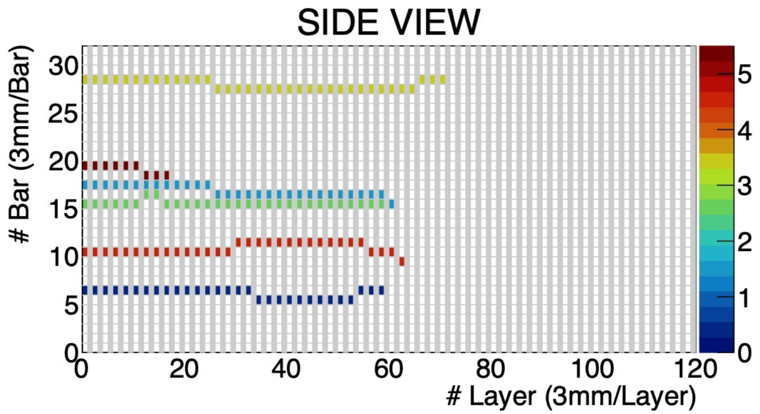
Ambiguities on multi-proton events

- The small crossectional area of the ASTRA bars allows multi-proton tracking but:
  - If two protons hit two layers of the detector two hits and two ghost hits (ambiguities) are generated
  - Both combinations of hits are indistinguishable





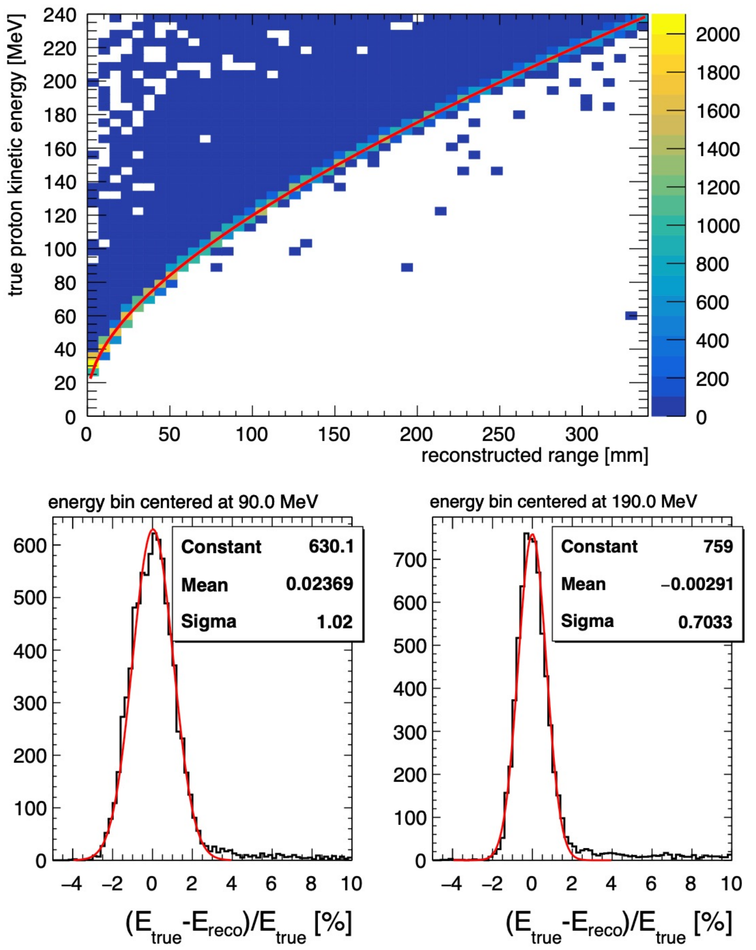




Energy reconstruction

- Energy reconstructed (purely by range) using range reconstructed by the length of each track.
- The use of 4 bits and 12 bits calorimetric information could help to improve the energy resolution and efficiency.
- Long tails due to hard scattering.

Segmentation → Length of track rather than depth/layer



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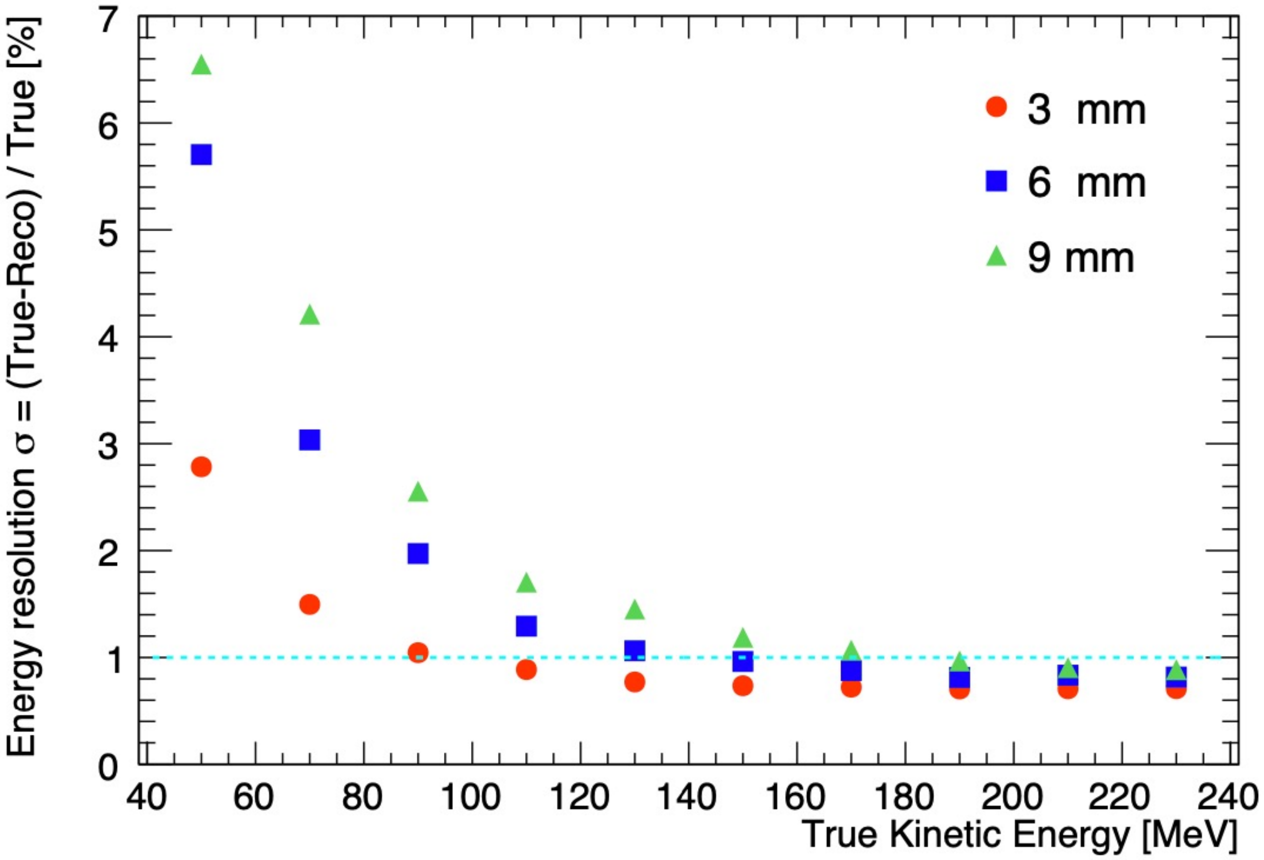
IFAE Institut de Física d'Altes Energies

Energy resolution

- Sub 1% resolution for protons above 100 MeV.
- The effect of the bars size is clear on low energy protons.
- 3 mm bars were used for the further studies.



Good protons

Not all protons that have a well reconstructed energy are protons **good for imaging (PGfI).**

Profiled energy on each pixel of a 200x200 grid with square pixels with 400 μm. Only the protons found within around the mean are accepted as good for imaging.

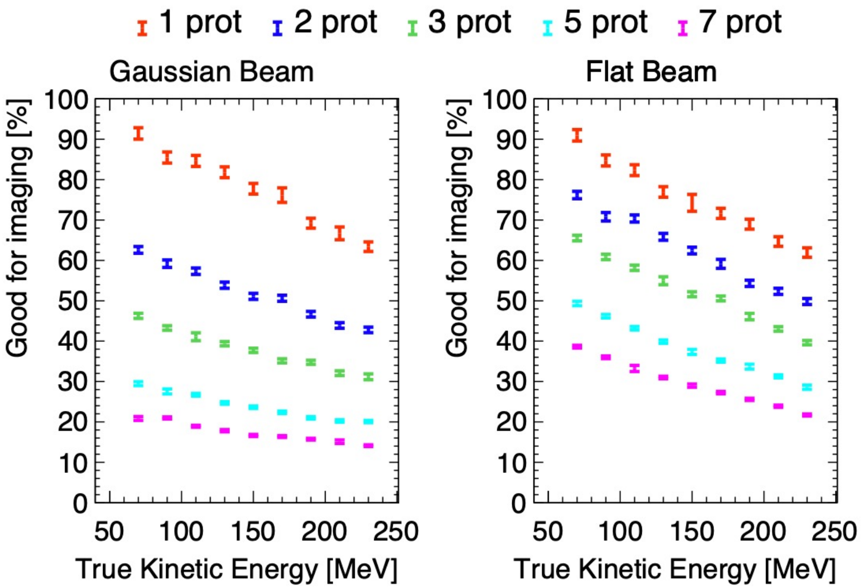
- Sub 1% resolution for protons above 100 MeV.

The beam profiles used were:

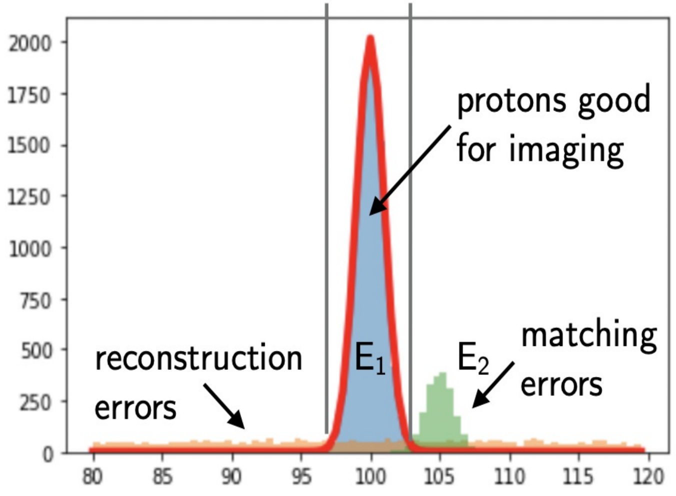
- Gaussian with σ **= 10 mm**
- 75 × 75 mm^2 square.

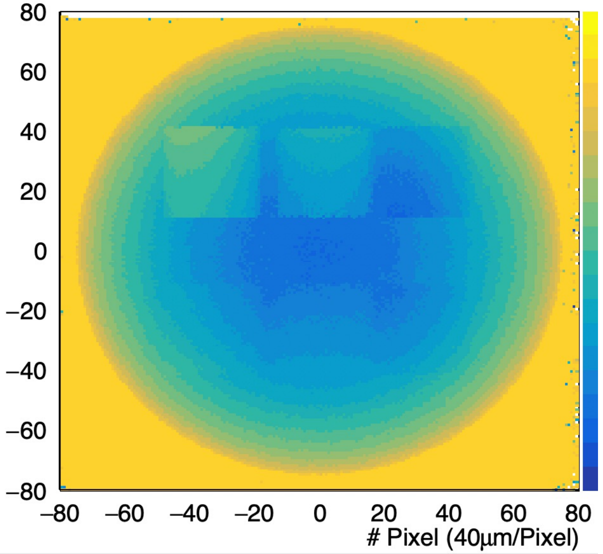
Two important factors:

- **Energy reconstruction**
- **Matching**



*idealized sketch

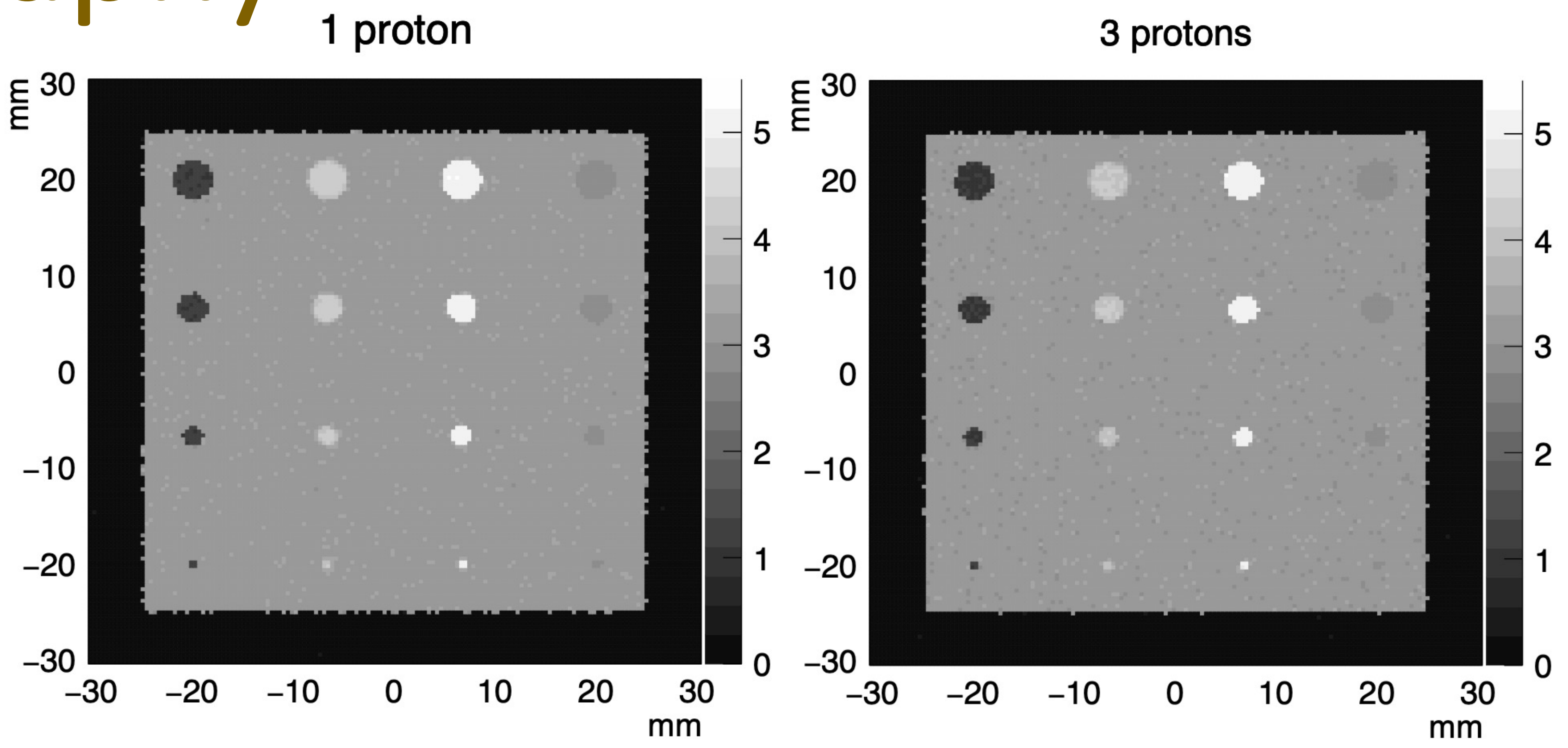




2D radiography

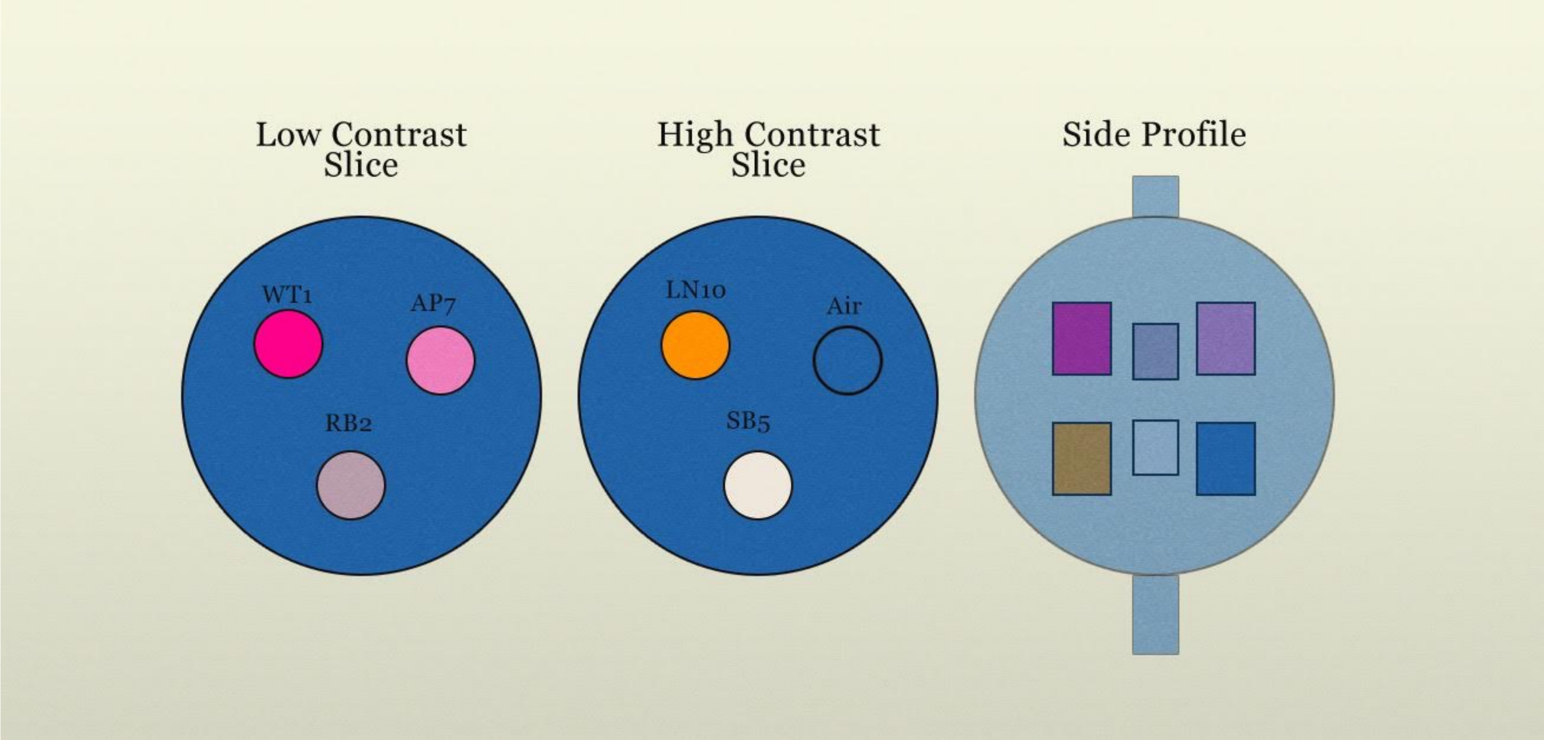
- Using gaussian beam σ=10mm.
- Phantom frame: water, inserts cylinders 3cm thick.
- Left to right: lung tissue, rib bone, hard cortical bone, and adipose tissue.
- Bottom to top: ø = 0.5, 1.0, 1.5 and 2 mm.

Material	Density [g/cm^3]
Water	1.00
Adipose	0.92
Lung	0.30
HC bone	1.84
Rib bone	1.40

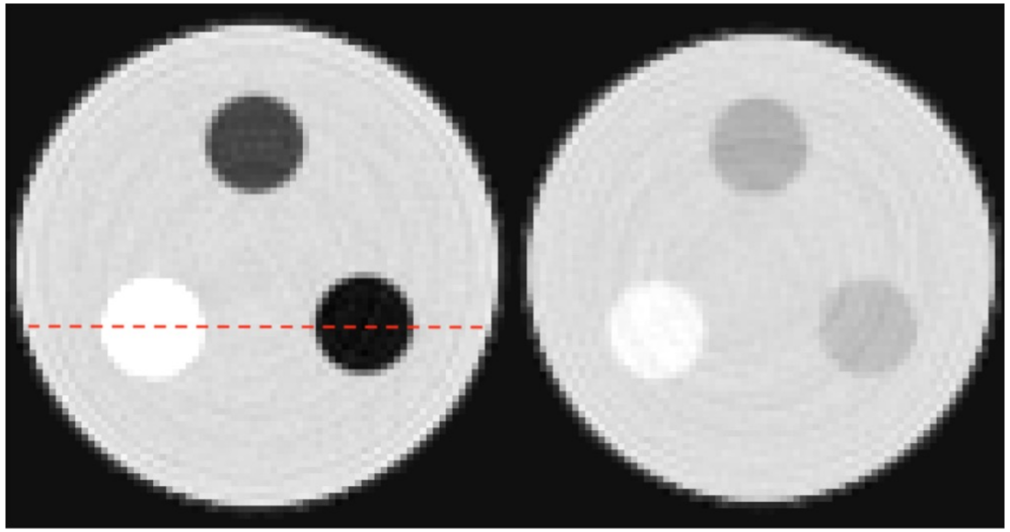


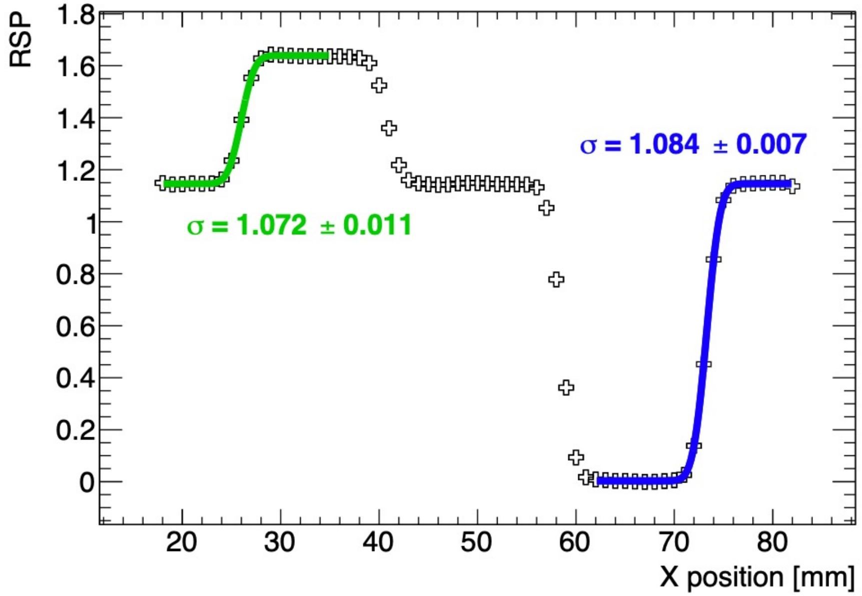
Associate position using DMAPS tracker using front projection to Z=0 plane and associate energy as reconstructed in ASTRA for that trajectory

The phantom



The 75 mm-diameter phantom used in simulations, representative of the experimental PRaVDA phantom: a PMMA sphere containing six cylinders, of cortical bone (SB5), lung (LN10), air, rib bone (RB2), adipose tissue (AP7) and water (WT1).





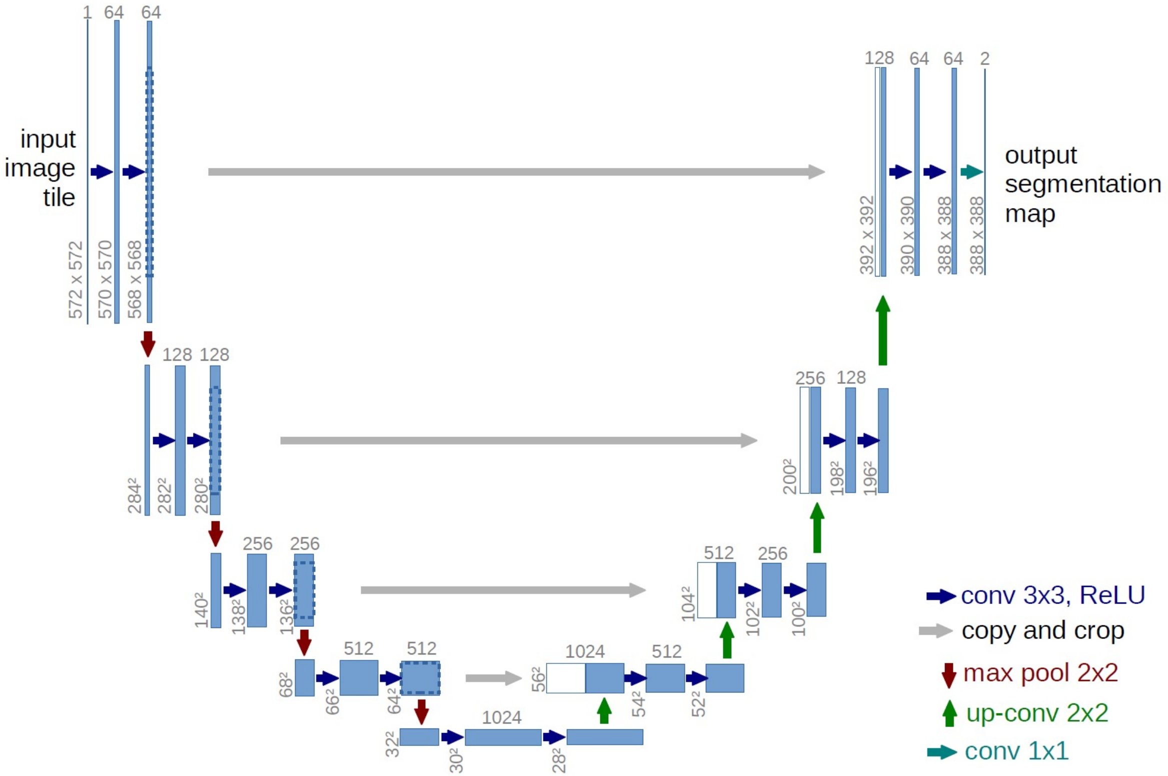
Material	RSP (Reco)	RSP (True)	%diff
Water	0.992 ± 0.002	0.994 ± 0.002	0.201
Air	0.009 ± 0.002	0.008 ± 0.002	-12.5
Adipose	0.916 ± 0.006	0.917 ± 0.005	0.109
Rib bone	1.325 ± 0.003	1.326 ± 0.001	0.075
HC bone	1.641 ± 0.003	1.646 ± 0.002	0.304
Perspex	1.144 ± 0.004	1.149 ± 0.002	0.455
Lung	0.302 ± 0.003	0.302 ± 0.002	0.000

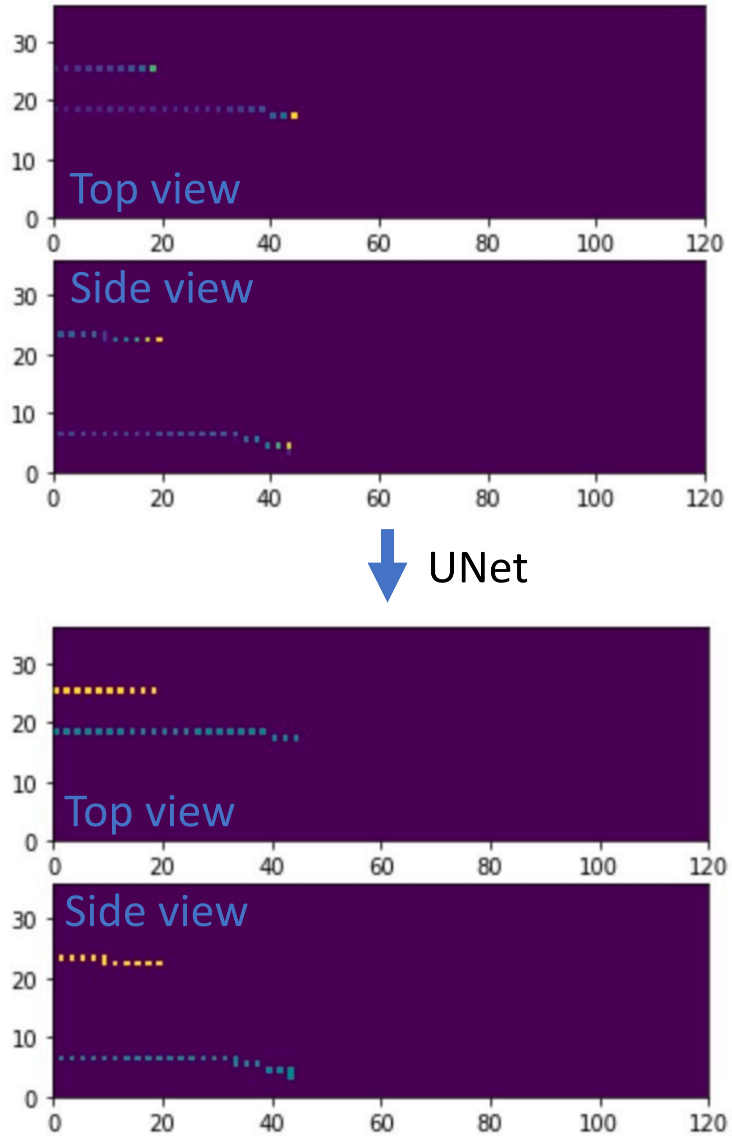
Material	RSP (Reco)	%diff (True)	%diff (1p)
Water	1.033 ± 0.002	3.924	4.133
Air	0.076 ± 0.006	850	744
Adipose	0.96 ± 0.02	3.60	3.71
Rib bone	1.34 ± 0.04	1.06	1.13
HC bone	1.66 ± 0.02	0.85	1.16
Perspex	1.14 ± 0.01	-0.78	-0.35
Lung	0.35 ± 0.02	15.89	15.89

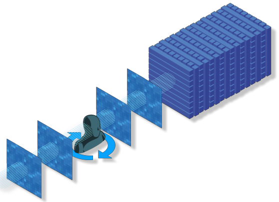
- High RSP contrast with 1 proton (<1% diff)
- Very good position resolution (~1mm)
- Mild degradation for 3 protons.

1 M events **2 protons** per event. **No phantom** and beam energies ranging between **80 to 180 MeV** to train a **UNet** using the edep information at each ASTRA bar.

1 M events with 1 proton to check with Classic Algorithms







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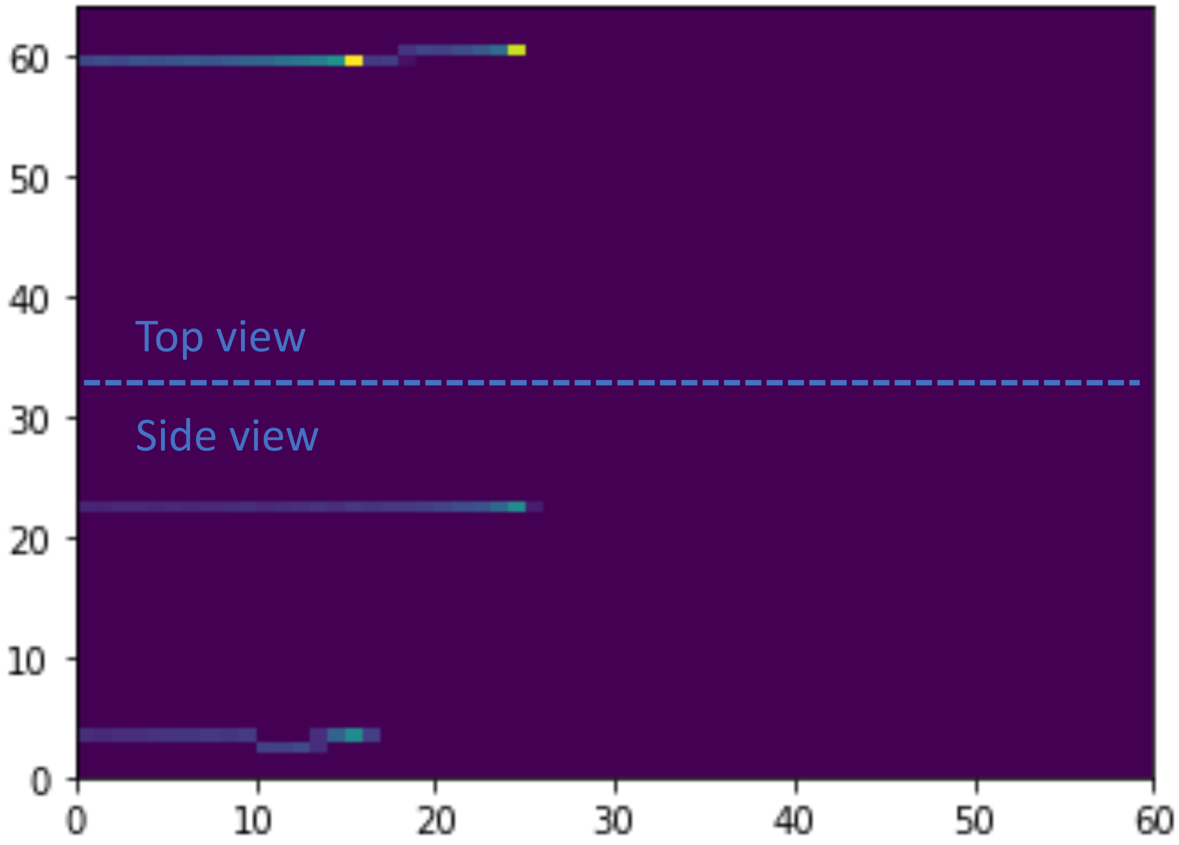
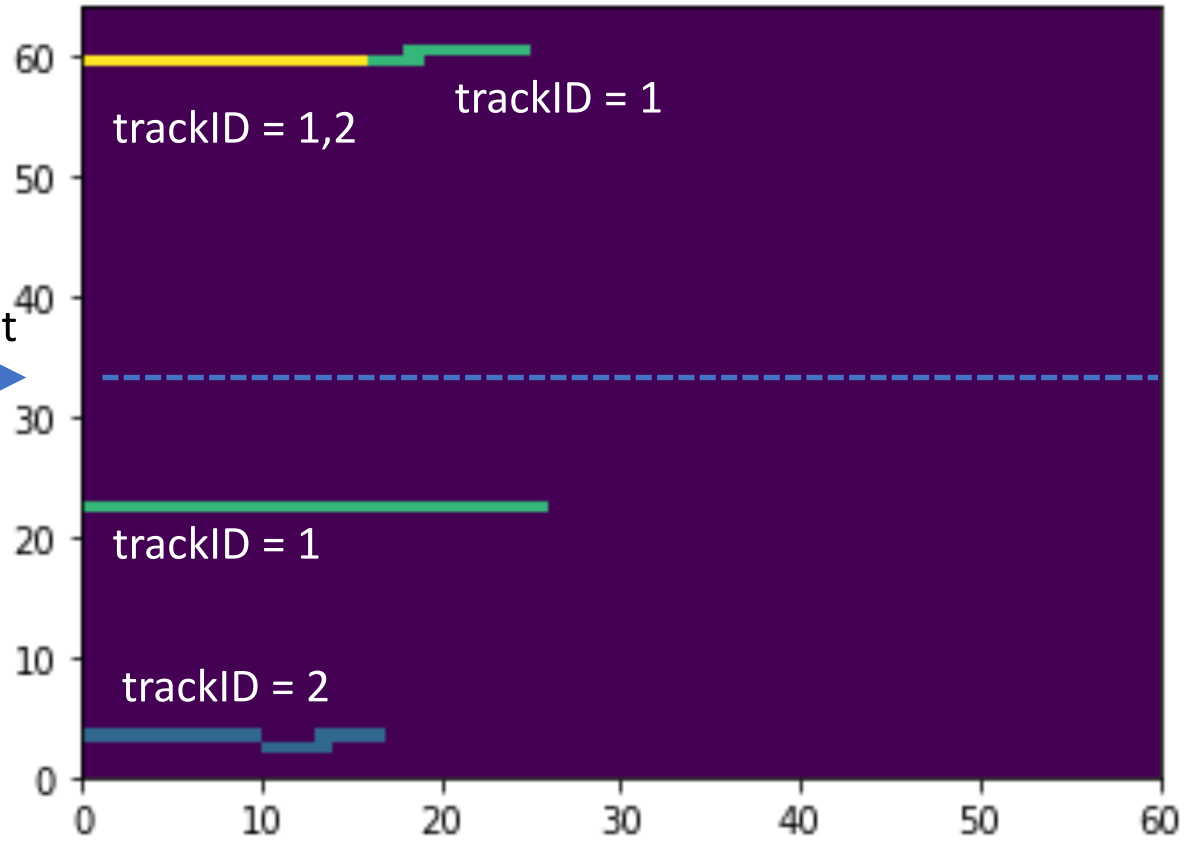
Input structure

- The input is the energy deposited (edep) and the output the different categories (track id = 1, 2 and overlap [1,2])
- The data is prepared into 60x64 pixel images merging vertical (top) and horizontal (bottom) projections.



UNet



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Reconstruction

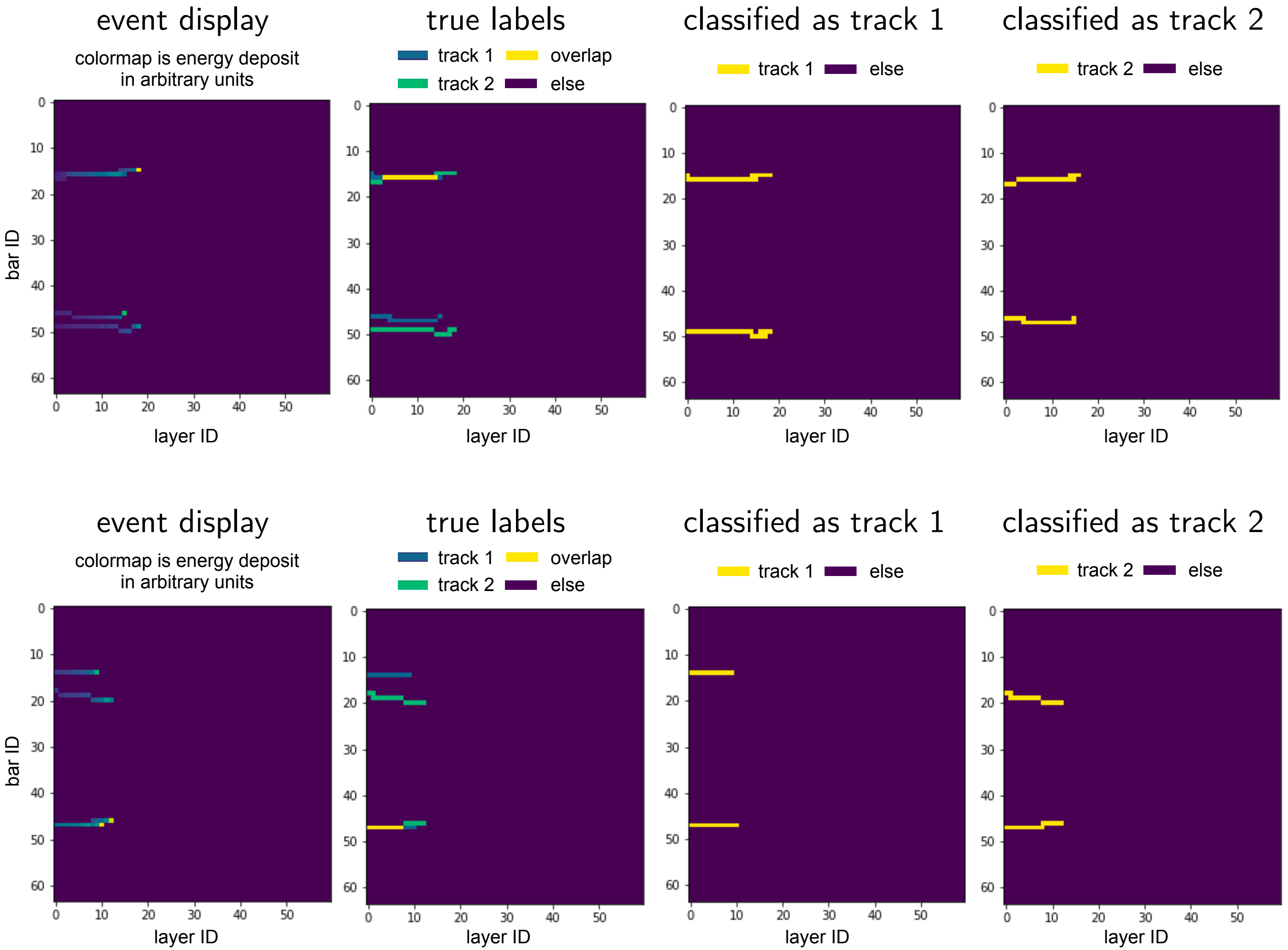
Signal segmentation with multi-label at pixel level!

Background = [1, 0, 0]

TrackID1 = [0, 1, 0]

TrackID2 = [0, 0, 1]

Overlap12 = [0, 1 ,1]



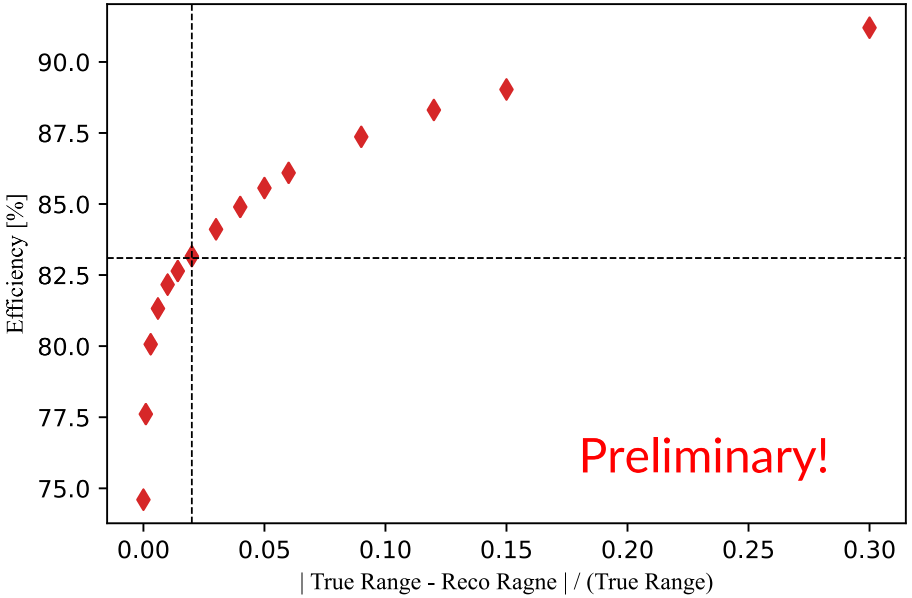
Efficiencies

Tracking efficiency an protons good for imaging (**pGfI**)

Algorithm	1p Track eff [%]	1p pGfI [%]	2p Track eff [%]	2p pGfI [%]
Classic	97	80	69	55
UNet	97	80	**82**	**68**

A **13 % improvement over all range of energies** is observed when using the Unet with 2 proton events.

Still **20 %** of the tracks are lost due to inelastic interactions. **Extra layer of NN to recover them!**

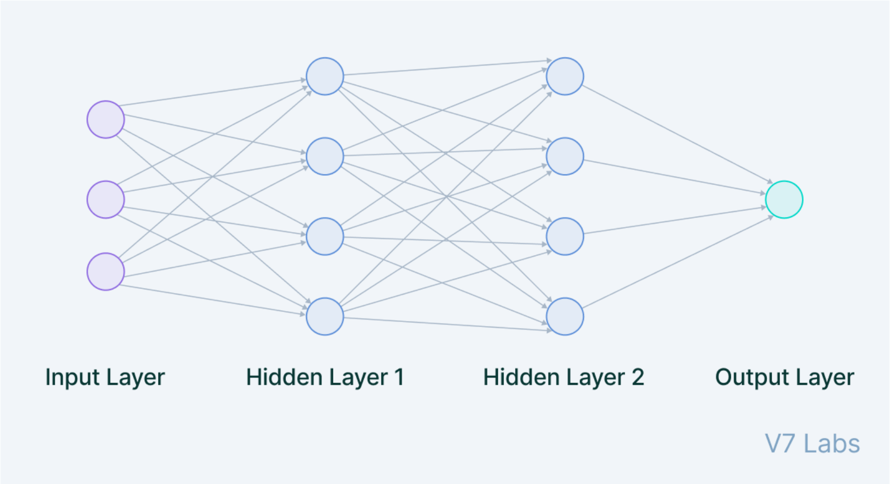


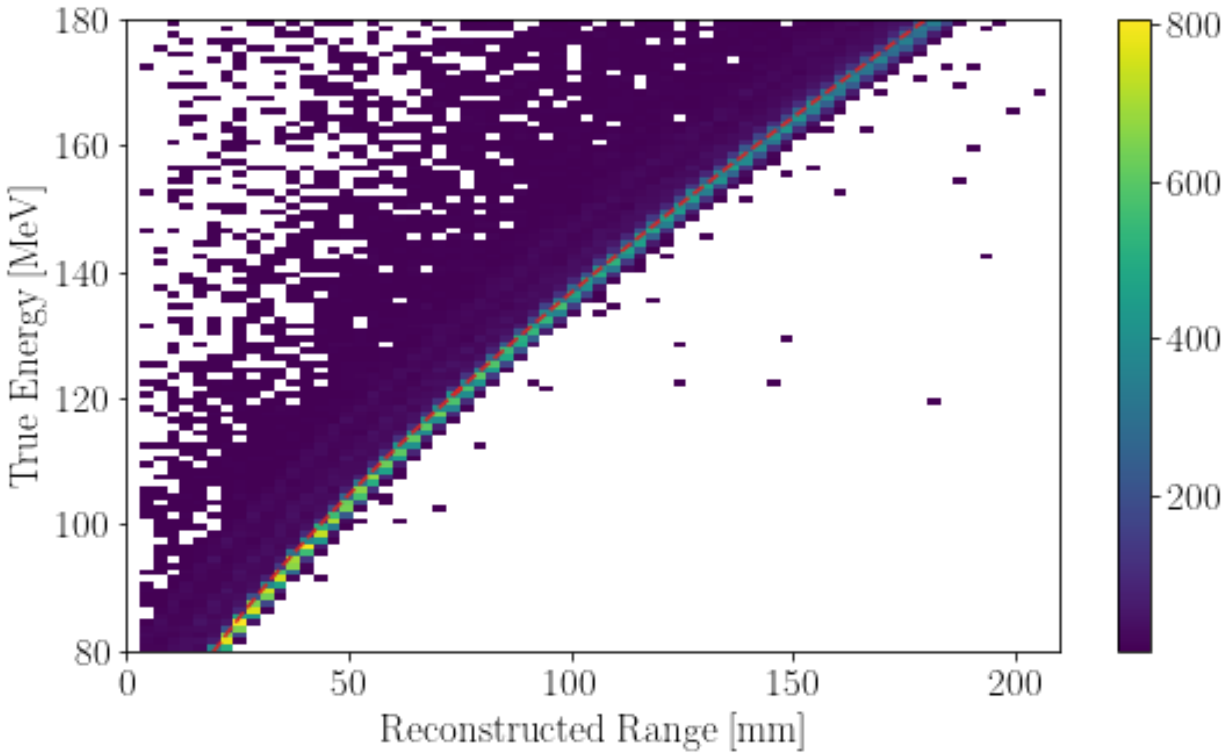
Proton selection for training the NN:

In order to perform a proper training the hits that suffer inelastic scattering.

Any good reconstruction of the energy obtained from these events would imply an increase in efficiency.

Use of NN for **regression problems**:





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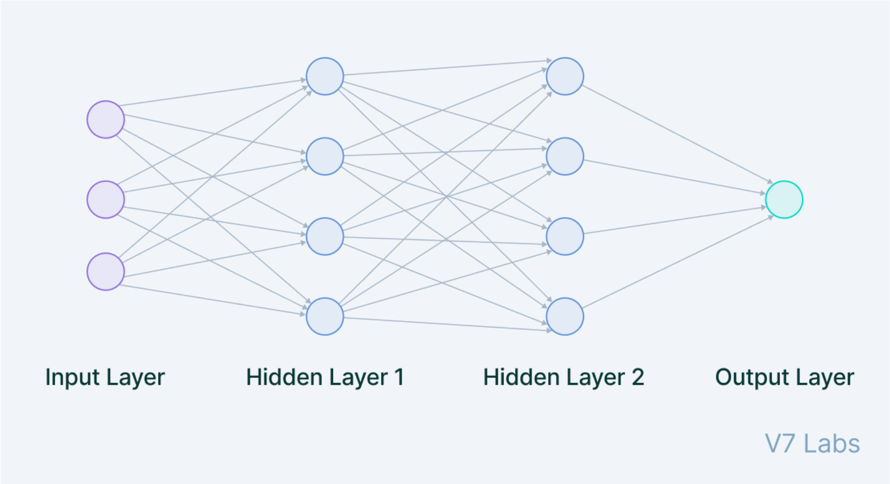
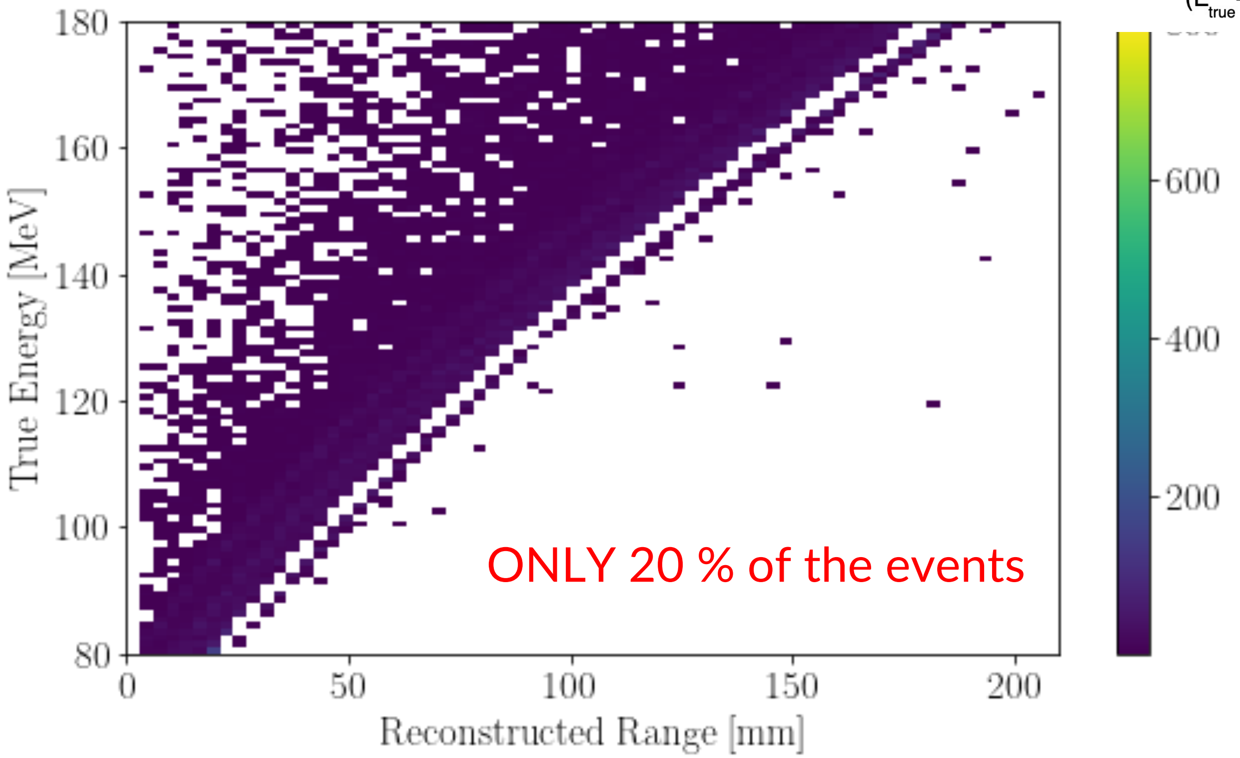
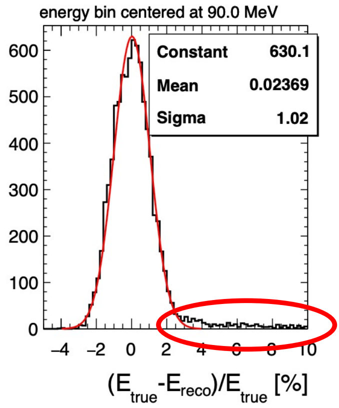




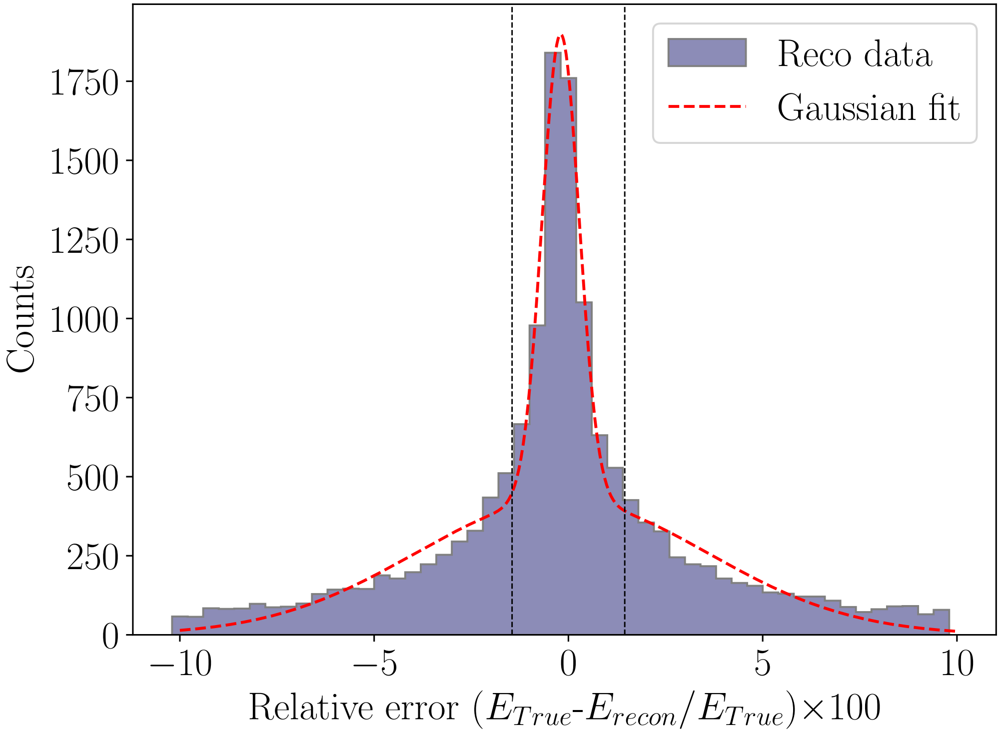


Efficiency of the NN for energy recontruction

The relative error has a small bias that can be easily corrected.

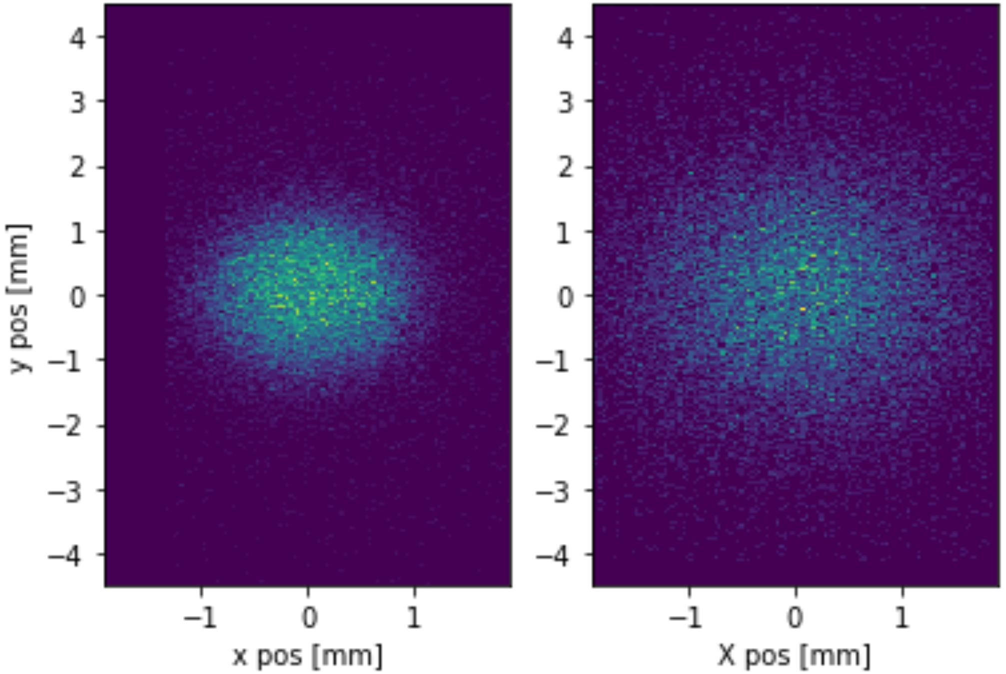
The sigma of the distribution is 1.65 %, very close to the 1 % resolution obtained with the "normal tracks".

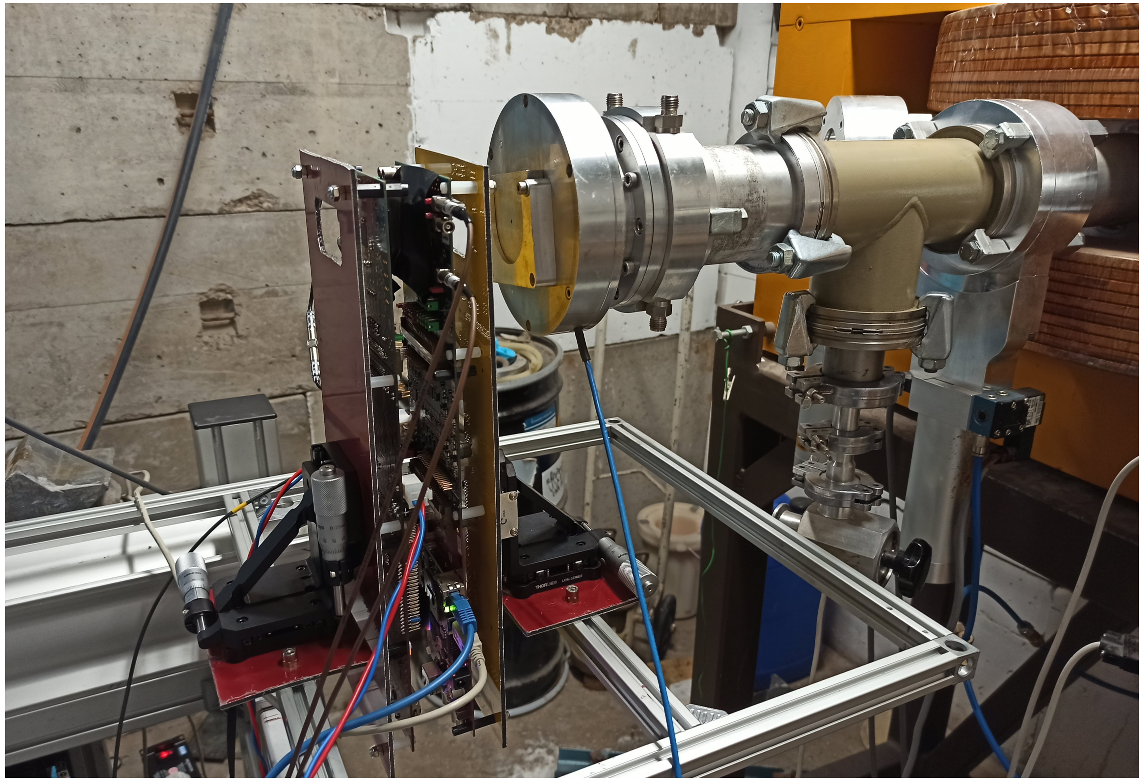
Taking $\pm\sigma$ (pGfI) 46 % of the rejected tracks are recovered **9.2 % improve in total efficiency**.



DMAPS Tracker in Birmingham

Two DMAPS setups were placed in front of a 28 MeV proton beam at 5 cm of a 2 mm collimator and spaced 4 cm apart. Beam aligned with the sensors and matched events even without sync options. Low energies -> Big scattering.





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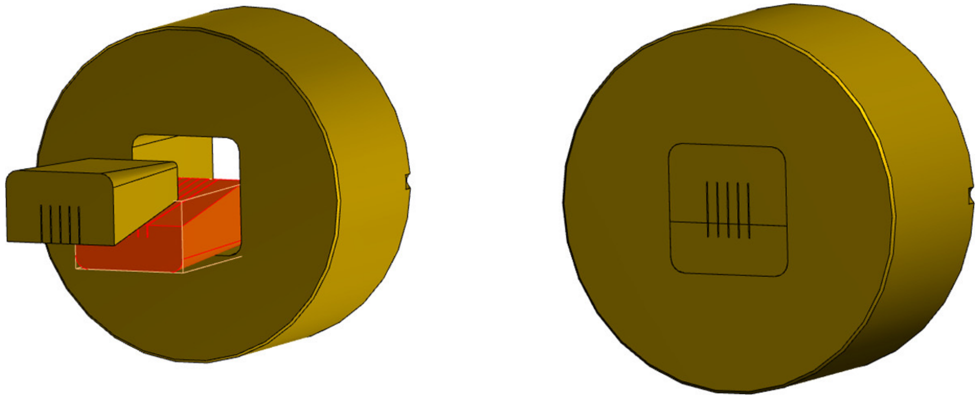
Test beam at pMBRT centre at CI

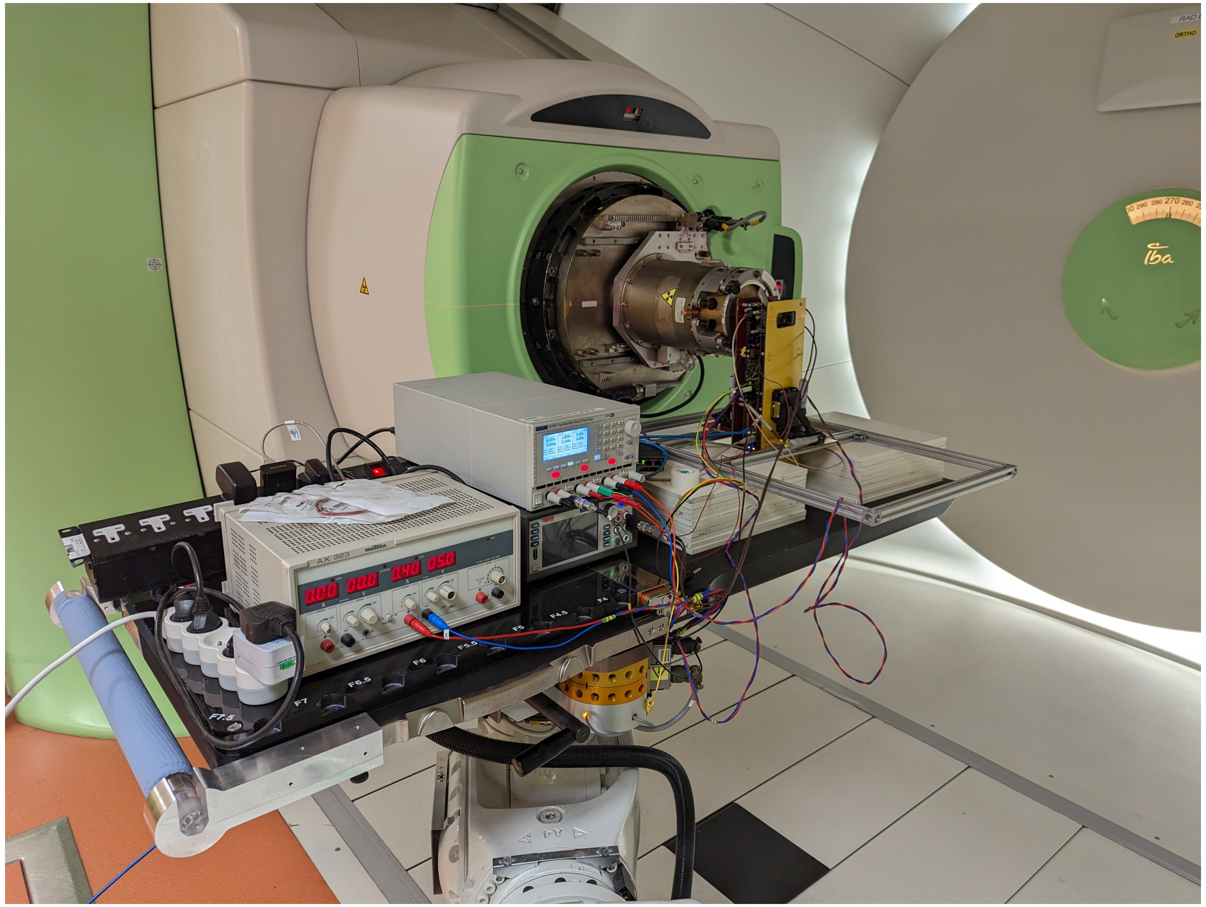
The pMBRT beamline at the CI offers the possibility of a high flux of 10^9 protons/cm^2/s with a small area.

Tracking protons for the first time at a clinical facility.

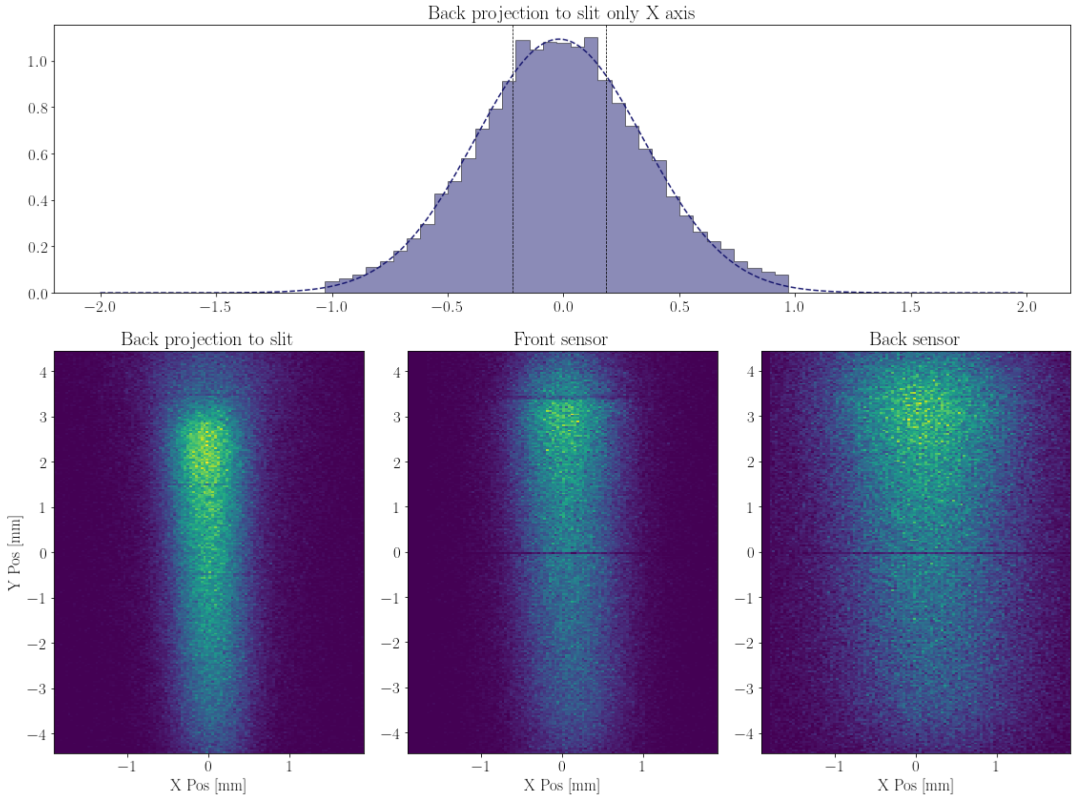
The collimator used for the test was a 5 cm cube of brass with a single slit with the dimensions of 0.4×20 mm^2



A single slit collimator was used for this test beam.



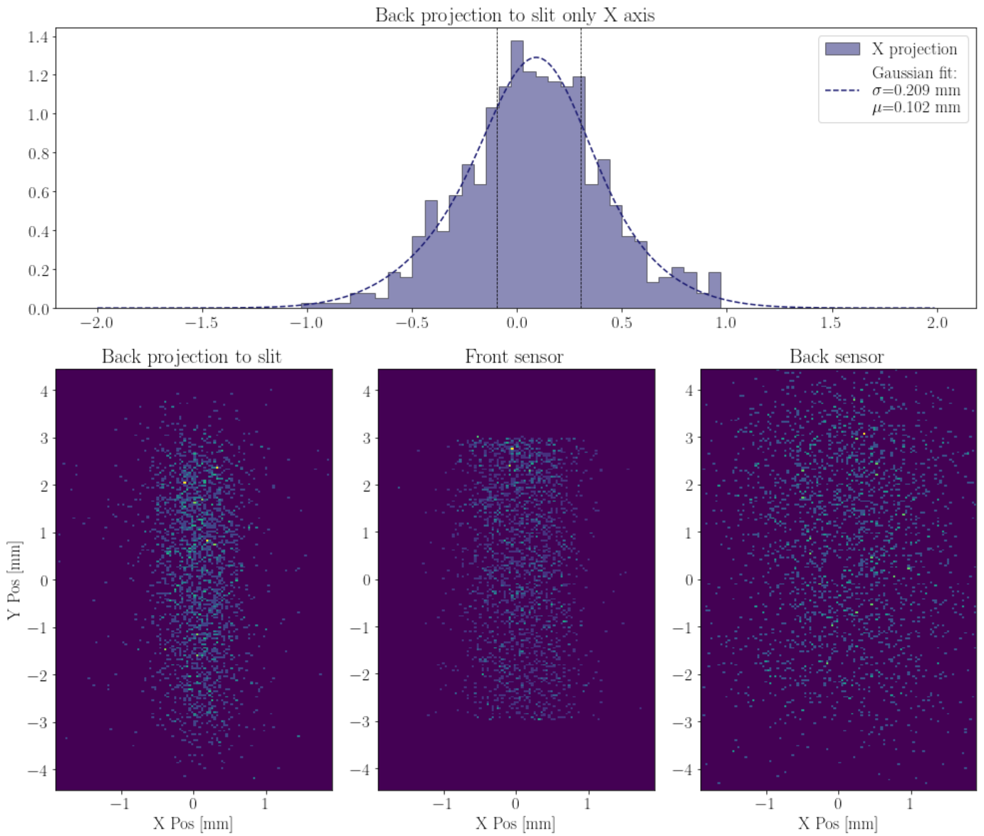
Back projection to slit



PRELIMINARY!

The tracked protons were back projected to the slit resulting in a Gaussian distribution along the X axis of 0.32 mm compared to the expected 0.18 mm regardless of a flat section shown between ±0.2 mm

Back projection with stronger cuts



PRELIMINARY!

VERY LOW EFFICIENCY!

Applying stronger cuts, a distribution with 0.2 mm sigma is obtained, as expected for 90 μm resolution.

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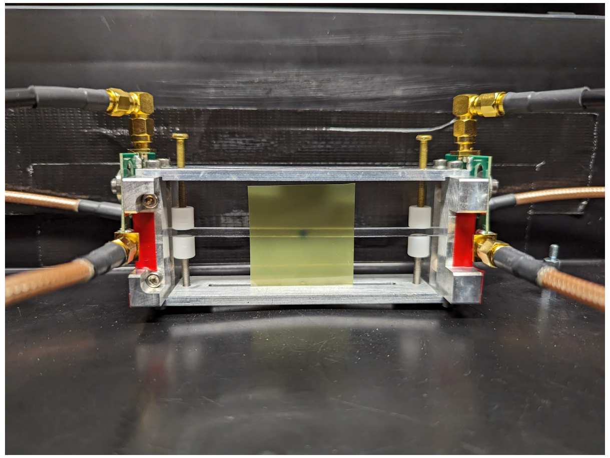
ASTRA Test beam MC40



The ASTRA plastic scintillating bars have been tested at the MC40 cyclotron

Lack of total internal reflection implies two things:

- If one SiPM is used on each side, one can obtain position information along the bar.
- If the geometry does not allow two-sided SiPM readout, coating or wrapping techniques will be needed to preserve the light.

Tests with foil wrapping are being done at the moment.

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Summary and conclusions

- Paper on arxiv: https://arxiv.org/pdf/2109.03452.pdf, published by Physics in Medicine & Biology
- Proton computed tomography is key in order to improve proton radiotherapy and increase the number of patients benefiting from it.
- The current systems are not fast enough to be used under clinical conditions or in clinical facilities
- The use of new technologies such as DMAPS and the suggested ASTRA system can be a big step forward in the field.
- A full Monte Carlo simulation has been built able to replicate all the relevant features of the proposed system.
- A preliminary analysis was performed to test the capabilities of ASTRA measuring the RSP of different materials within a phantom.
- The images obtained present an excellent material contrast and a spatial and RSP resolution needed
- The TJ-Monopix chip was used to track protons at a clinical facility for the first time.
- The University of Birmingham, University of Geneva and IFAE are working on collaboration to develop the ASTRA system applying for funding to build a prototype and test it at Birmingham's MC40 cyclotron and other clinical beams in the following years to proof the capabilities of this technology

Thanks for your attention!

Acknowledgements:

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University of Birmingham EPSRC Impact Accelerator Account

STFC Global Challenge Network + in Advanced Radiotherapy Town Meeting

By: STFC Global Challenge Network+ in Advanced Radiotherapy

institut Curie

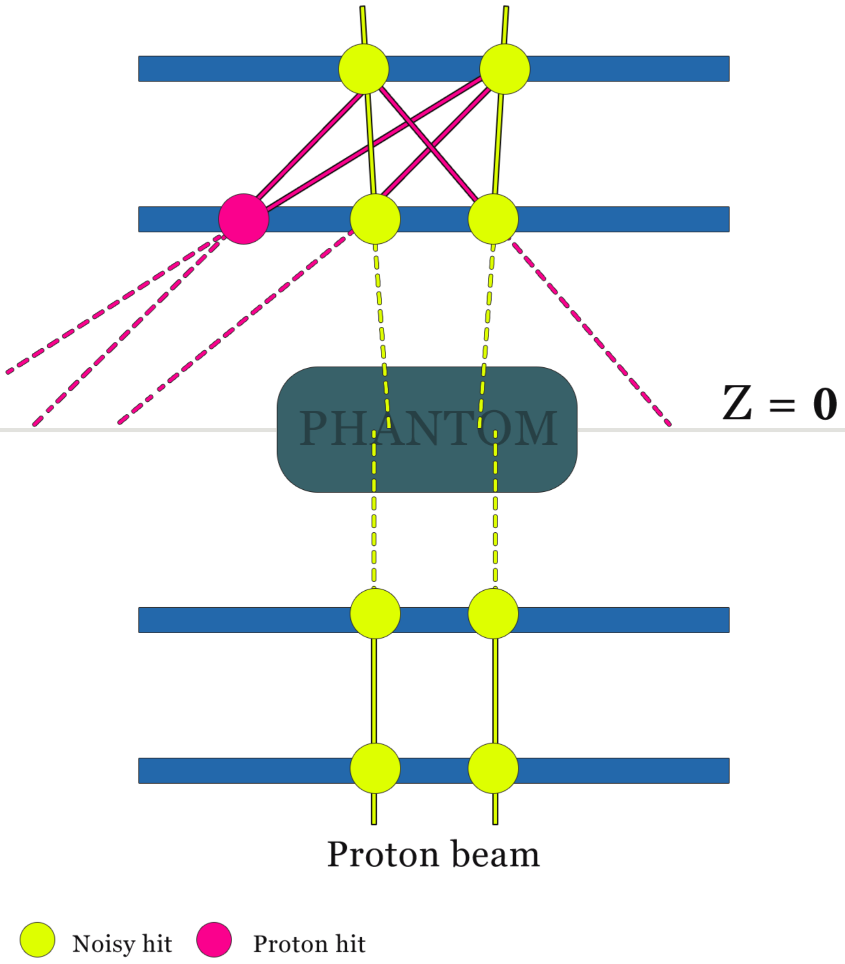
Backup

Matching tracks

The XY distance between front and back projections at Z = 0 as the key parameter to select the tracks in multi proton events.

This results in a rise of the purity in matching front and back tracks, when finding 2.

The tracking algorithm builds all possible 3D lines with hits in 2 first planes, same in the 2 last planes, look for combinations of lines (4 points) that minimize global χ^2(to straight lines) for single proton events.



Efficiency and purity

The figure of merit for the front tracker is $Purity \times Efficiency$ defined as:

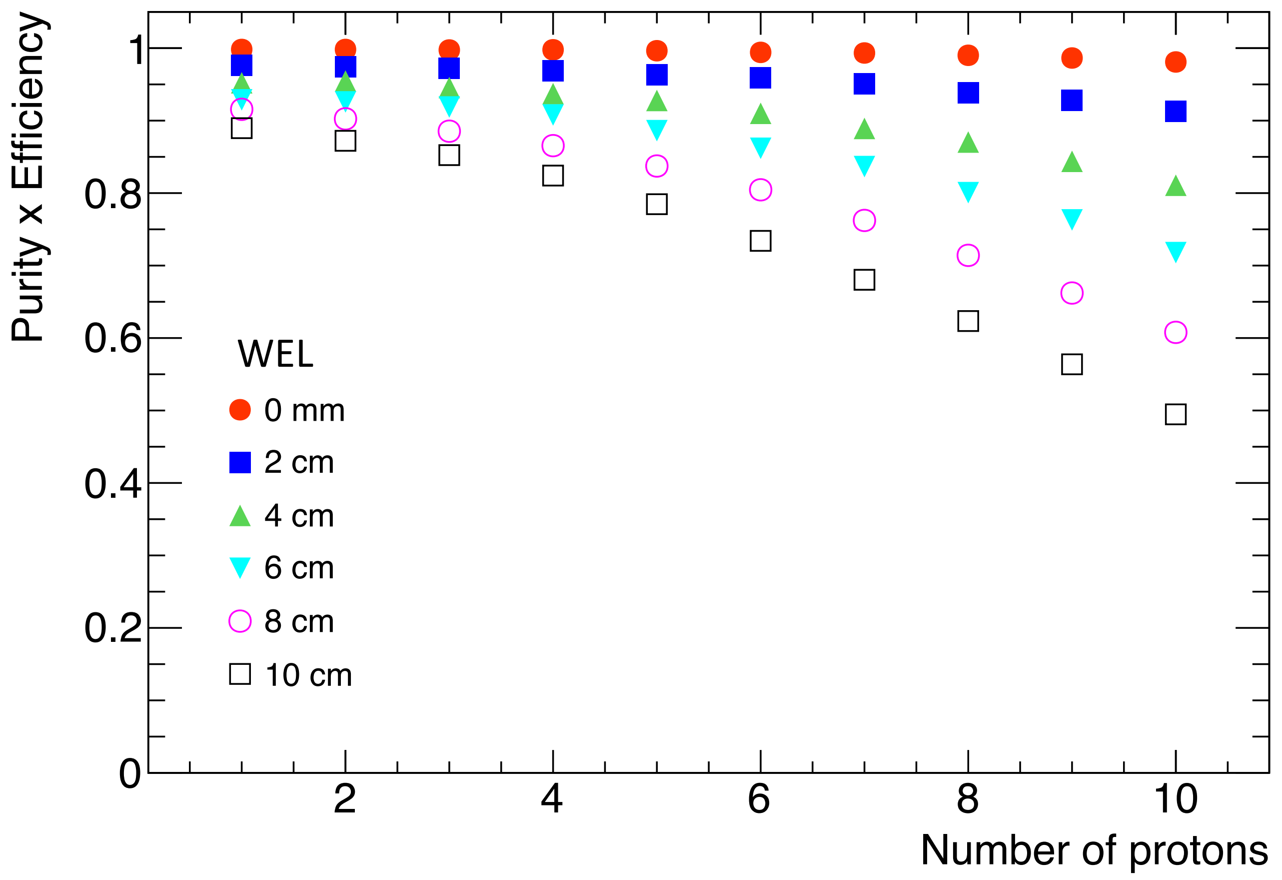
$$Purity = \frac{Well\ Reco\ Tracks}{Total\ Reco\ Tracks}$$

$$Efficiency = \frac{Total\ Reco\ Tracks}{Total\ \ Tracks}$$

Plotted as function of the number of protons per event for different water equivalent lengths (WEL).

180 MeV protons with a Gaussian beam distribution with $\sigma = 10\ \text{mm}.$

Note that MCS will affect on the efficiency (lost protons) and purity (crossed tracks).

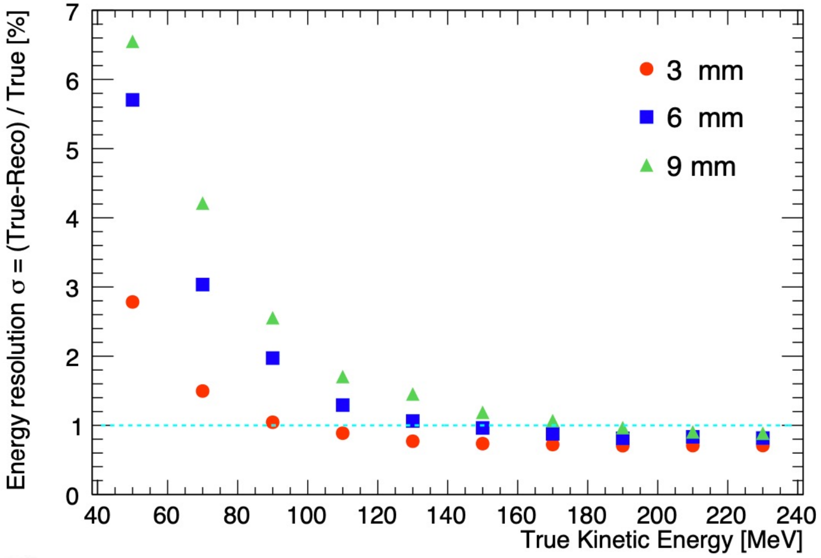


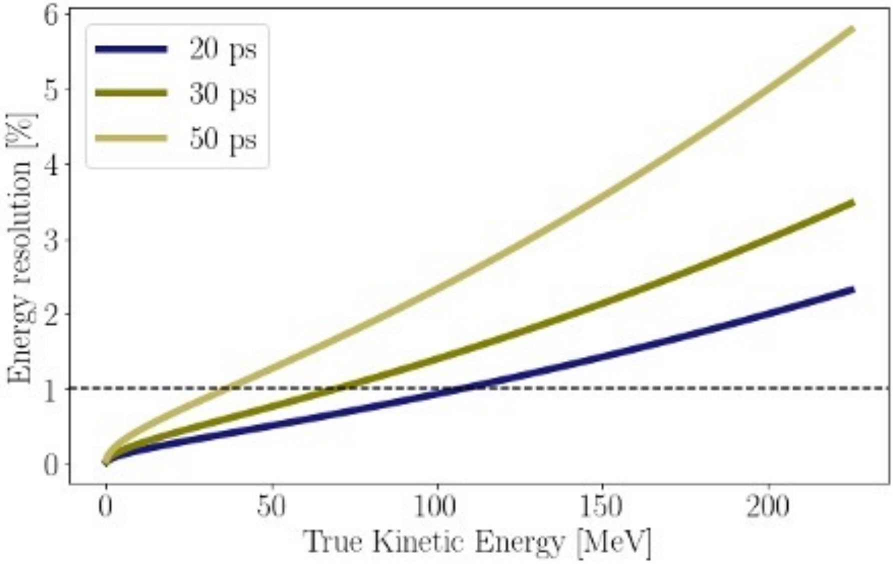
Current work

The use of other pixel technologies could improve the performance of whole the system.

Fast timing pixels could improve the resolution of the PSP by adding three important factors:

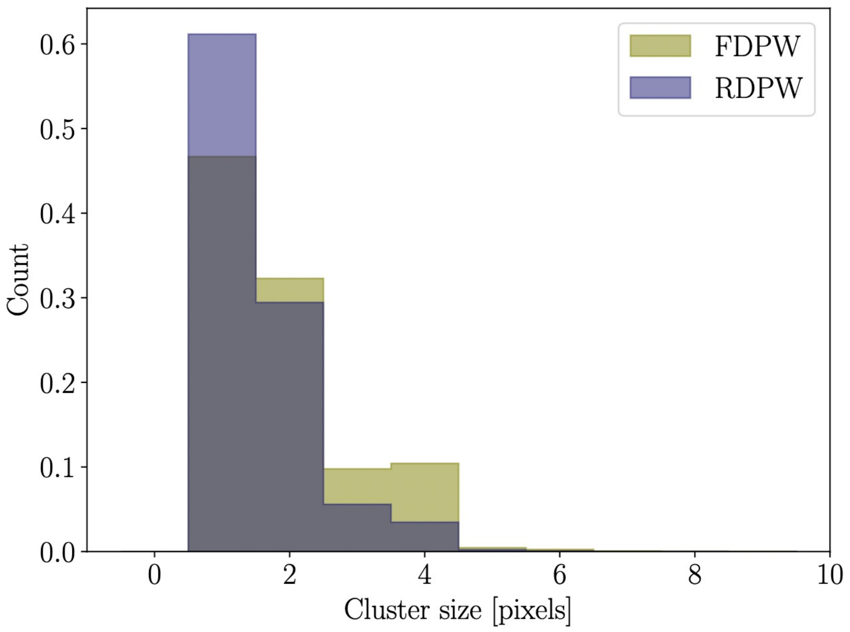
- Higher multi proton efficiency for tracking
- Measurement of the individual proton's energy before entering the body by ToF.
- Covering the low energy range where the ASTRA's resolution is compromised → maybe even make ASTRA redundant?

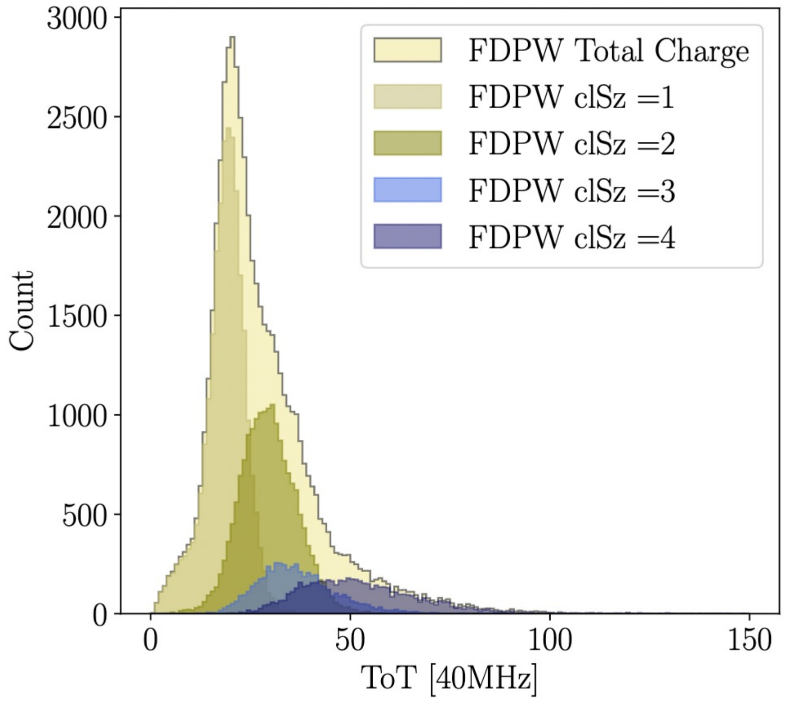


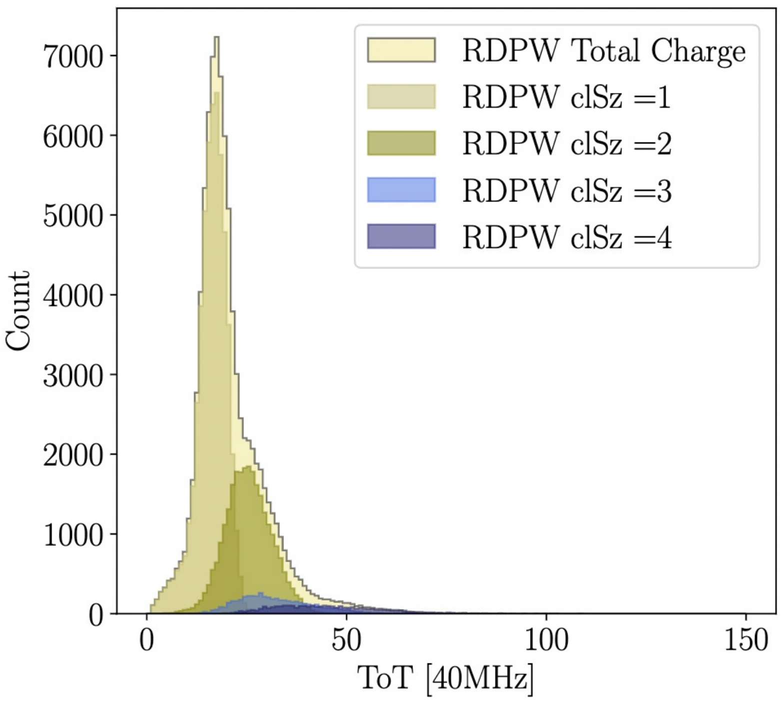


Charge reconstruction

At the higher energies of the pMBRT line, the cluster size recovers the expected decaying shape. Charge reconstruction follows the expected Landau.







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