Monte Carlo methods and application in hadron therapy

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Outline

- Introduction: what is hadron therapy?
- Positron Emission Tomography
- Monte Carlo simulations in hadron therapy
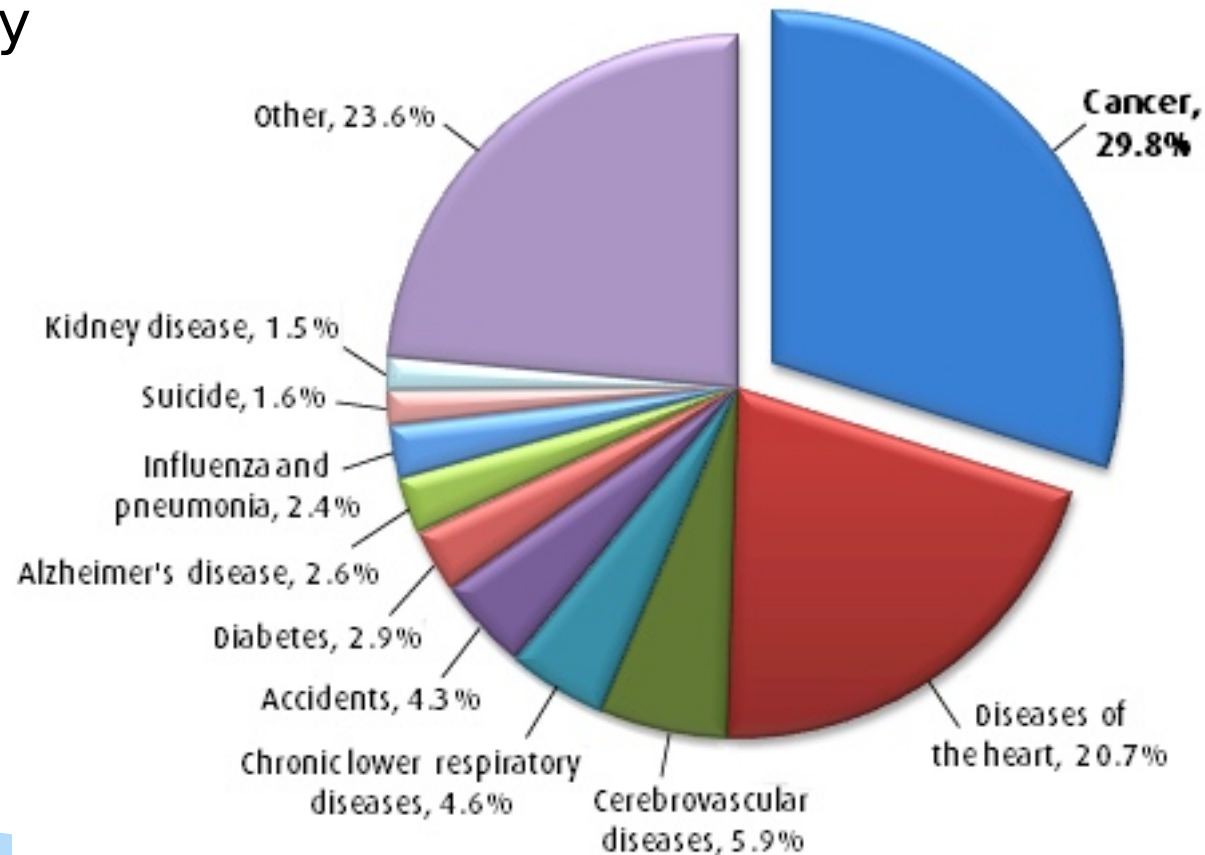- Data taking: CNAO and CATANA
- Conclusion

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  - Cancer treatment, hadron therapy
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Cancer treatment

- Cancer: one of leading causes of death in developed countries

- Treatment with:
  - Chemotherapy
  - Operation
  - Radiation therapy

Proportion of Deaths Due to Cancer and Other Causes, Canada, 2009

Other, 23.6%

Cancer, 29.8%

Kidney disease, 1.5%

Suicide, 1.6%

Influenza and pneumonia, 2.4%

Alzheimer's disease, 2.6%

Diabetes, 2.9%

Accidents, 4.3%

Chronic lower respiratory diseases, 4.6%

Cerebrovascular diseases, 5.9%

Diseases of the heart, 20.7%

Radiotherapy

- Photon therapy (x-ray), most conventional
- Electrons, mostly for superficial coverage
- Heavy charged particles, like protons, carbon, ecc: new!
 - NB: I focus mostly on protons
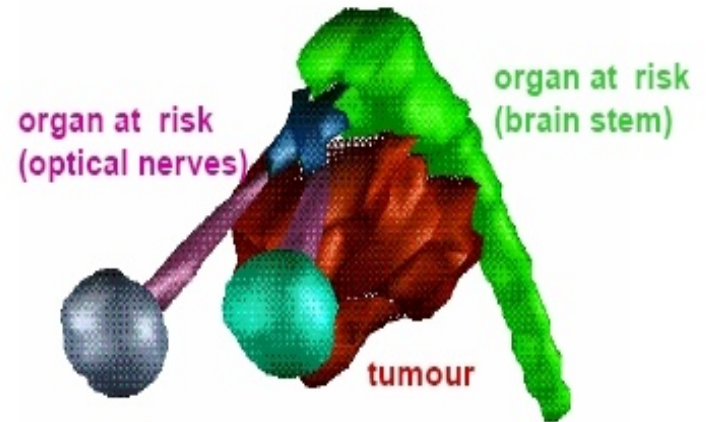
Purposes:

- Deliver a high dose to tumoral tissue

- **"Conformal" dose distribution** on the target volume

- Spare as much as possible health tissues and "Organs at Risk"

organ at risk (optical nerves)
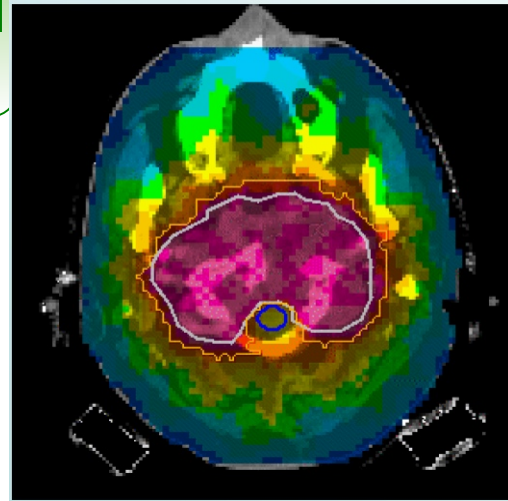
organ at risk (brain stem)

tumour
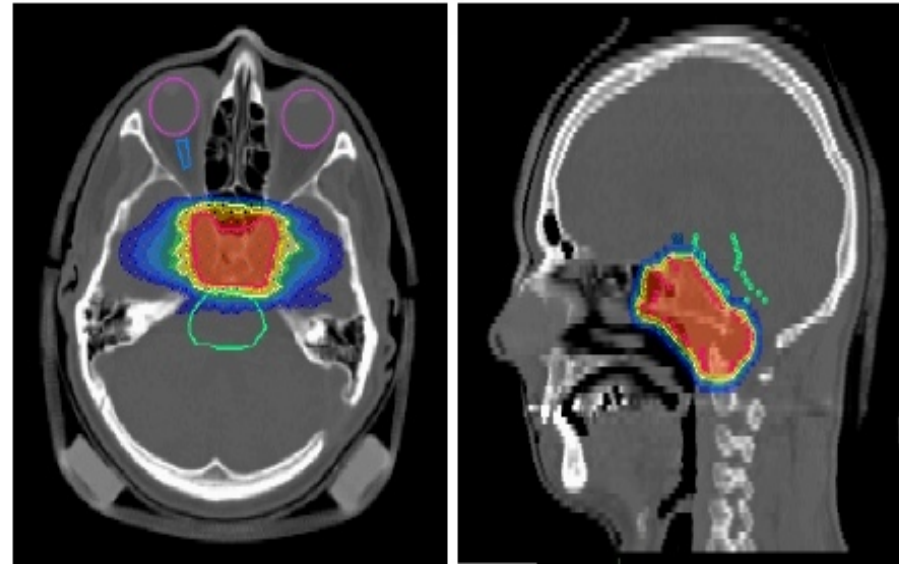
Why hadron therapy?

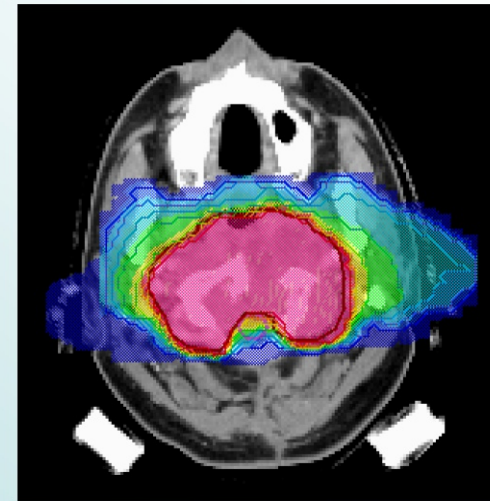Charged particles have highly advantageous dose profile compared to photons!

Photons: high dose delivered in front and behind tumor
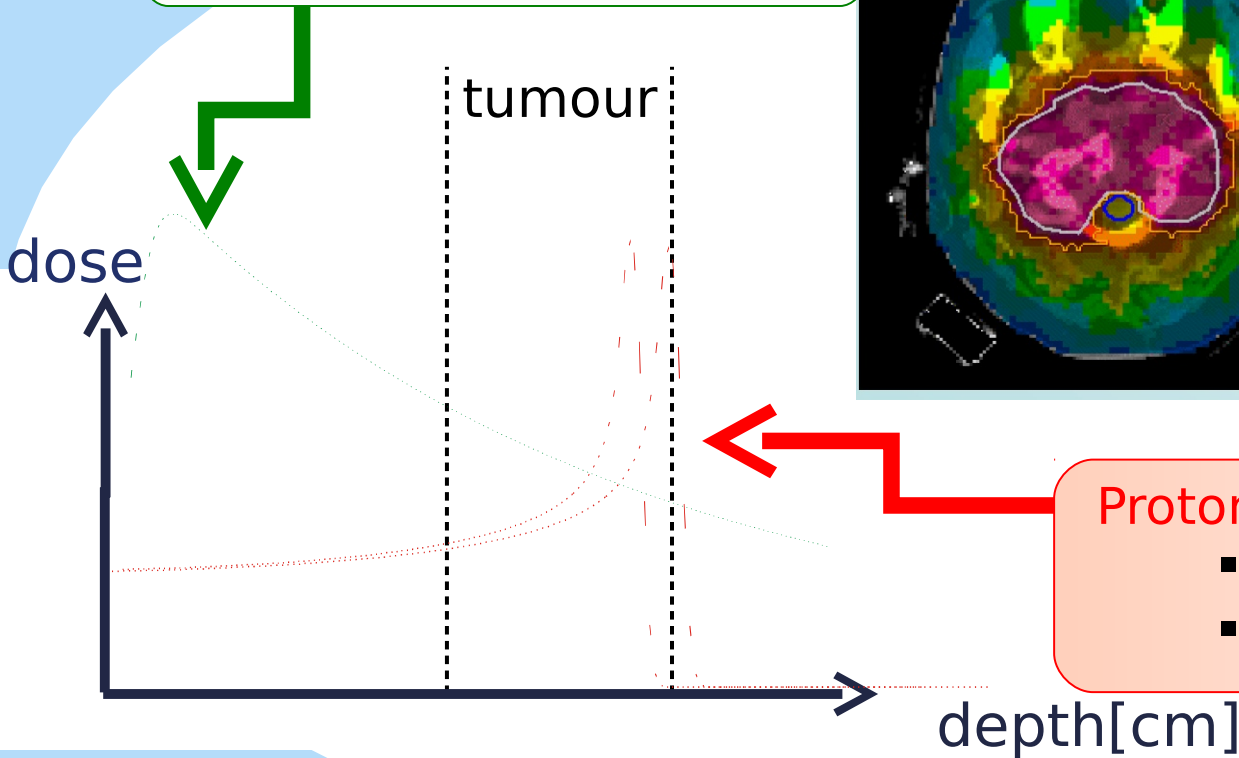
IMRT: 9 Fields

Carbon ions: 2 Fields

dose

tumour

depth[cm]

Protons: Bragg Peak: Dose spot
- Energy ~ depth
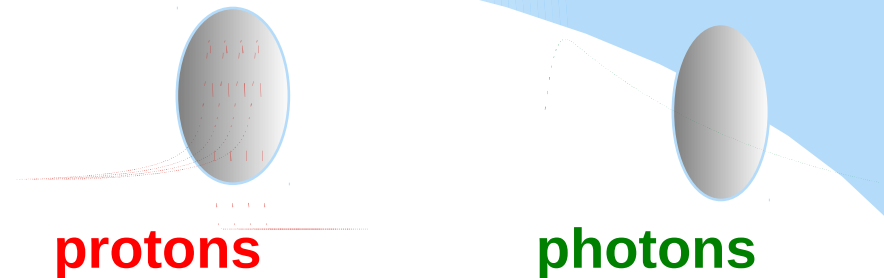- Nr. protons ~ height

Reminder: dose [Gy]=Energy [J]/mass [kg]

Necessity for dose monitoring

Plan CT

One of the main disadvantages of charged particle therapy is the sensitivity to uncertainties:

- Steep dose gradients
- Matching of many

individual pencil-beams

protons   **photons**

- **Anatomical changes:** (internal organ motion, changes in air cavities, tumour regression, weight loss
- **Proton range** (calibration CT apparatus, proton stopping power, implants)
- **Patient inter-fractional setup** (daily positioning on the couch)

If we miss the target (for whatever reason) we can cause a damage...

(much more serious than for photons)

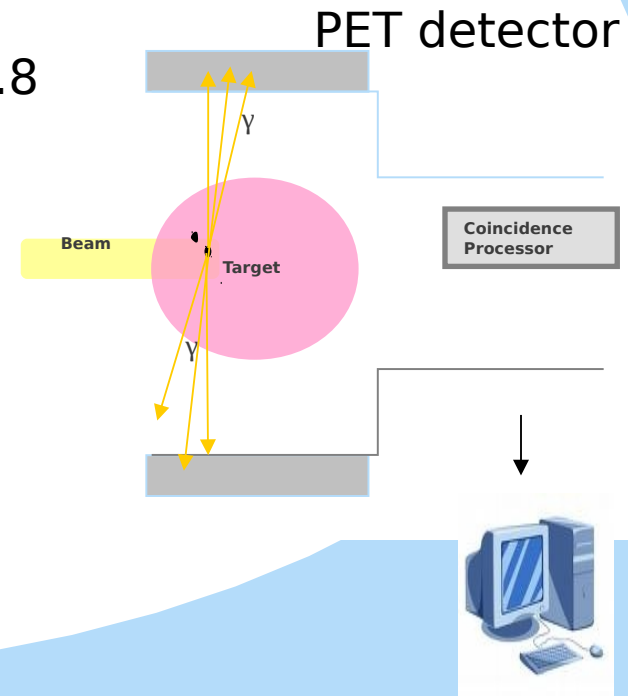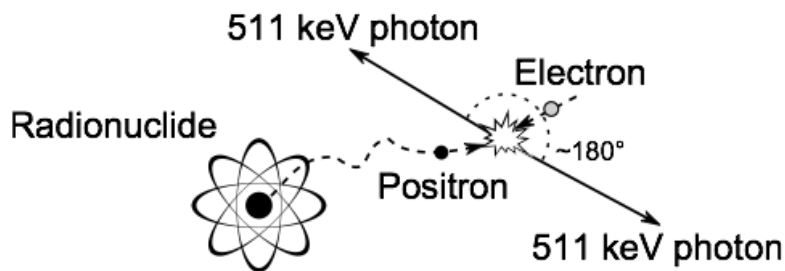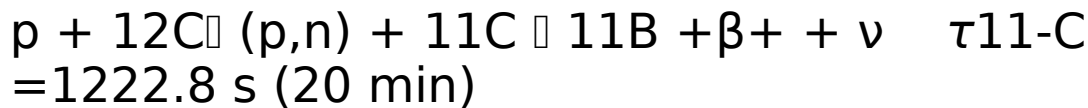It would be good, if we could monitor the range of the protons!

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Positron Emission Tomography

- One of the most promising ways to verify the delivered dose is by means of PET (Positron-Emission-Tomography)

- Therapeutic hadron beams produce β+ emitters in the body

Activity=nr of radioactive decays per time-interval
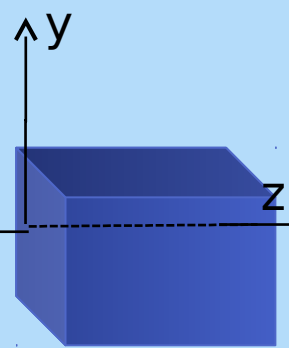
E.g. proton beam:

p + 16O $\rightarrow$ (p,n) + 15O $\rightarrow$ 15N +β+ + ν τ15-O=121.8 s (2 min)

p + 12C $\rightarrow$ (p,n) + 11C $\rightarrow$ 11B +β+ + ν τ11-C =1222.8 s (20 min)

PET detector

511 keV photon

Electron

Radionuclide

~180°

Positron

511 keV photon

Beam

Target

Coincidence Processor

γ

γ

Activity

MC simulation 58 MeV protons on PMMA
- Dose deposition ⬜ 3-D spatial distribution
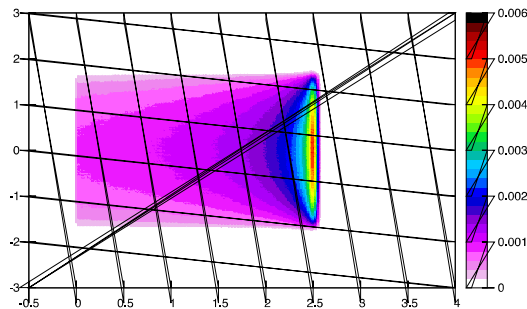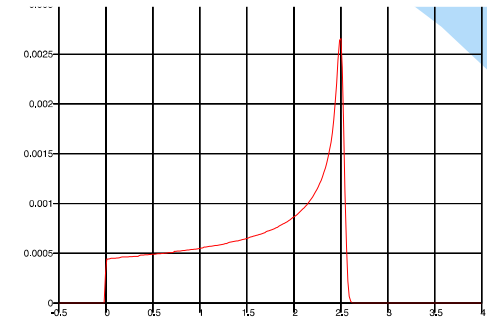- Production of B+ emitters ⬜ 3-D spatial distribution

proton

Dose

2-D

2-D: projected on yz

1-D
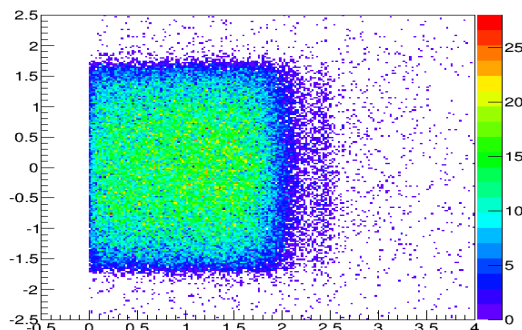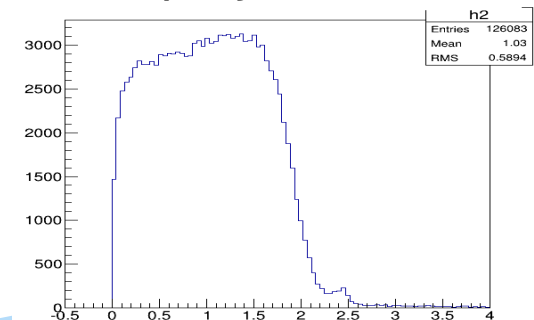
1-D: projected on z

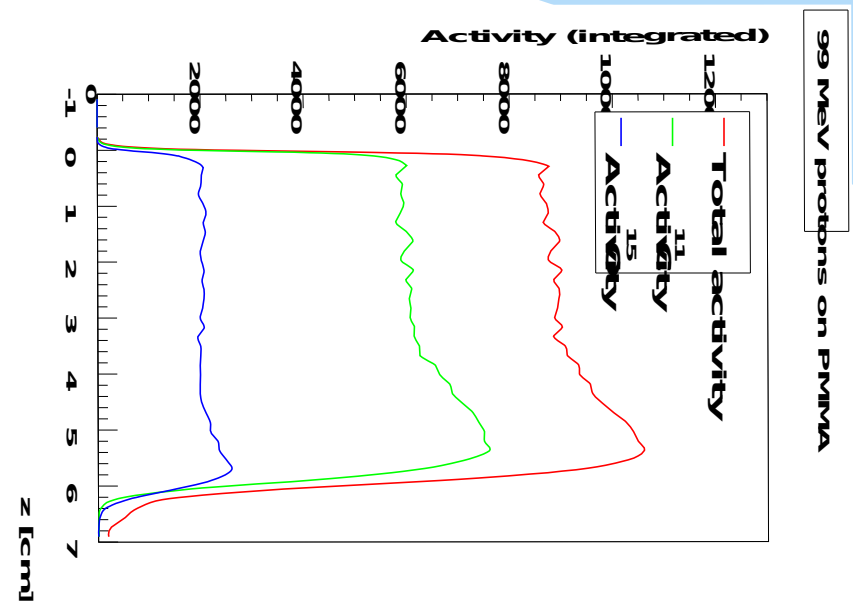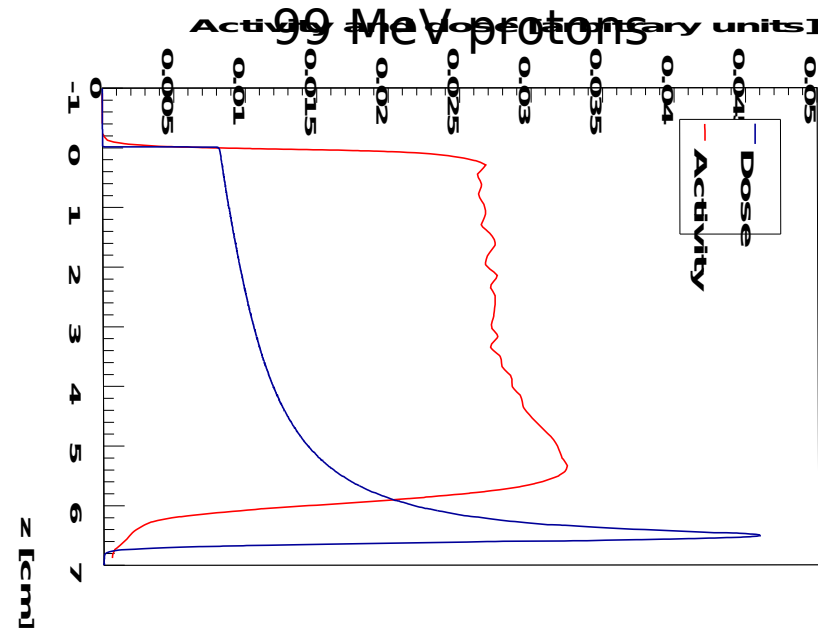**β+ emissions (activity)**

2-D: projected on yz

1-D: projected on z

Dose and activity

If we can measure the activity profile with PET, we have *indirect* information about the dose!

- It comes for free (patient is radioactive anyway)
- Even though the information is indirect, comparing the predicted Monte Carlo profile with the measured profile gives indications about the correctness of the dose delivery!

The final goal

MC dose calculation

- First developed by Parodi etal, applied in Heidelberg

- Now Pisa is working together with the Centro Nazionale di Adroterapia Oncologica (Pavia) and CATANA (Catania) to realize a treatment control system.
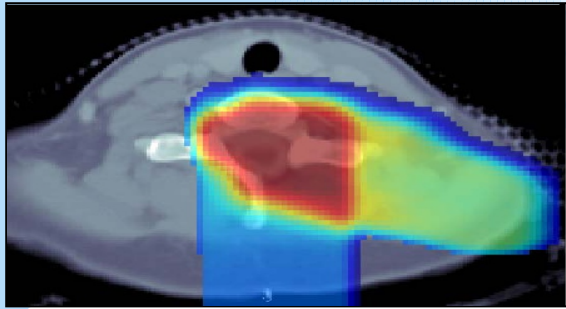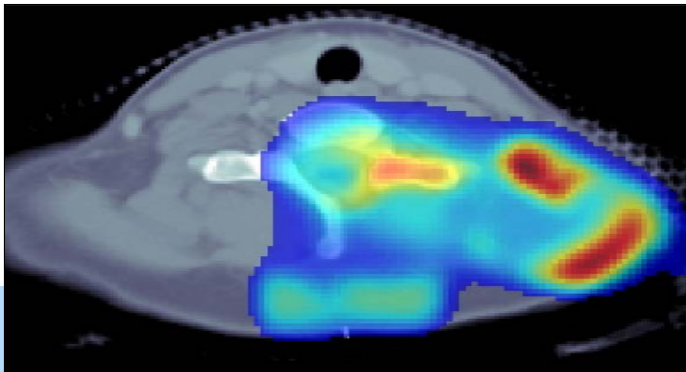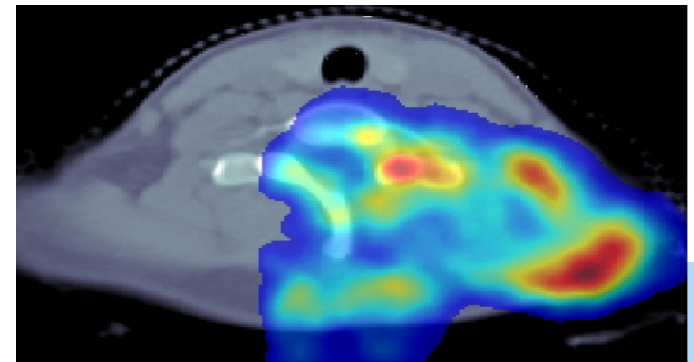
Treatment plan: set of pencil beams

MC expected PET activity (2D)

Measured PET activity (2D)

comparison

ACTION?

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Monte Carlo simulations

- Tool to calculate energy, dose, activity in materials

- Compare MC with data to check the underlying physics

- Realistic description of particle interactions, especially in complex geometries and inhomogeneous media where analytical approaches are at their limits of validity

- Study quantities that you cannot measure directly

- Startup and Commissioning of new particle therapy facilities: e.g., shielding calculations; beamline modeling

The ideal Monte Carlo generator

For a monitoring system of dose/range for hadron therapy, what does an
ideal Monte Carlo code need to do?

✓ Excellent description of most important proton
(0-300 MeV) interactions on target
  ✓ Electromagnetic
  ✓ Hadronic

✓ Excellent prediction
  of beta+ activity
  spatial distribution

✓ It should be user-friendly

✓ It should not be too slow

http://www.fluka.org
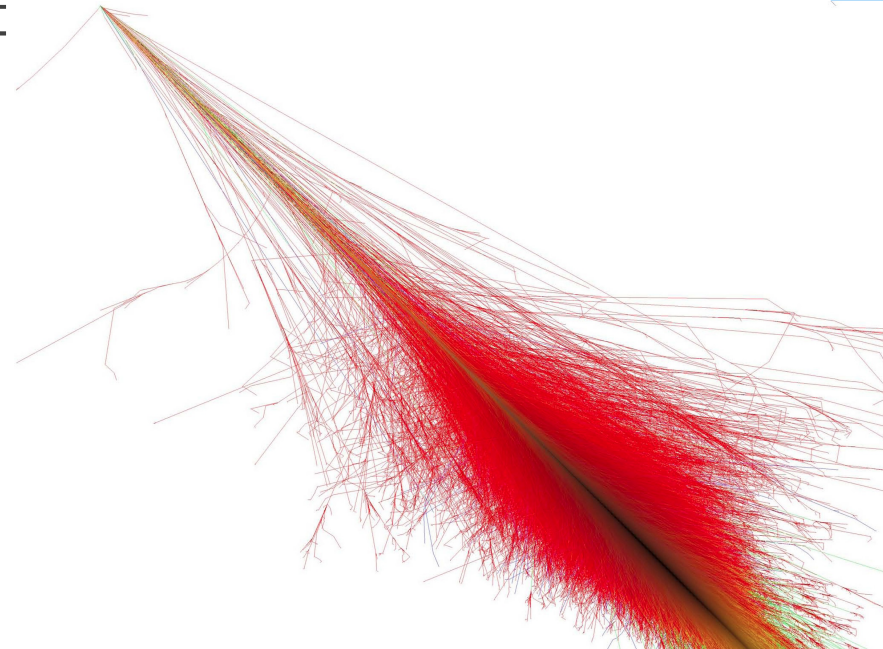
The FLUKA Monte Carlo generator

An example of a good Monte Carlo code for hadron therapy is FLUKA

- Hadron-hadron and hadron-nucleus interactions 0-100 TeV
- Electromagnetic interactions 0-100 TeV
- Charged particle transport including all relevant processes
- Code written in FORTRAN (user friendly)
- Beginning of FLUKA: 1962 (!)

In the following:

- FLUKA description of electromagnetic+nuclear interactions (general)
- PET activity simulations (my own code and simulations, work in progress)

http://www.fluka.org

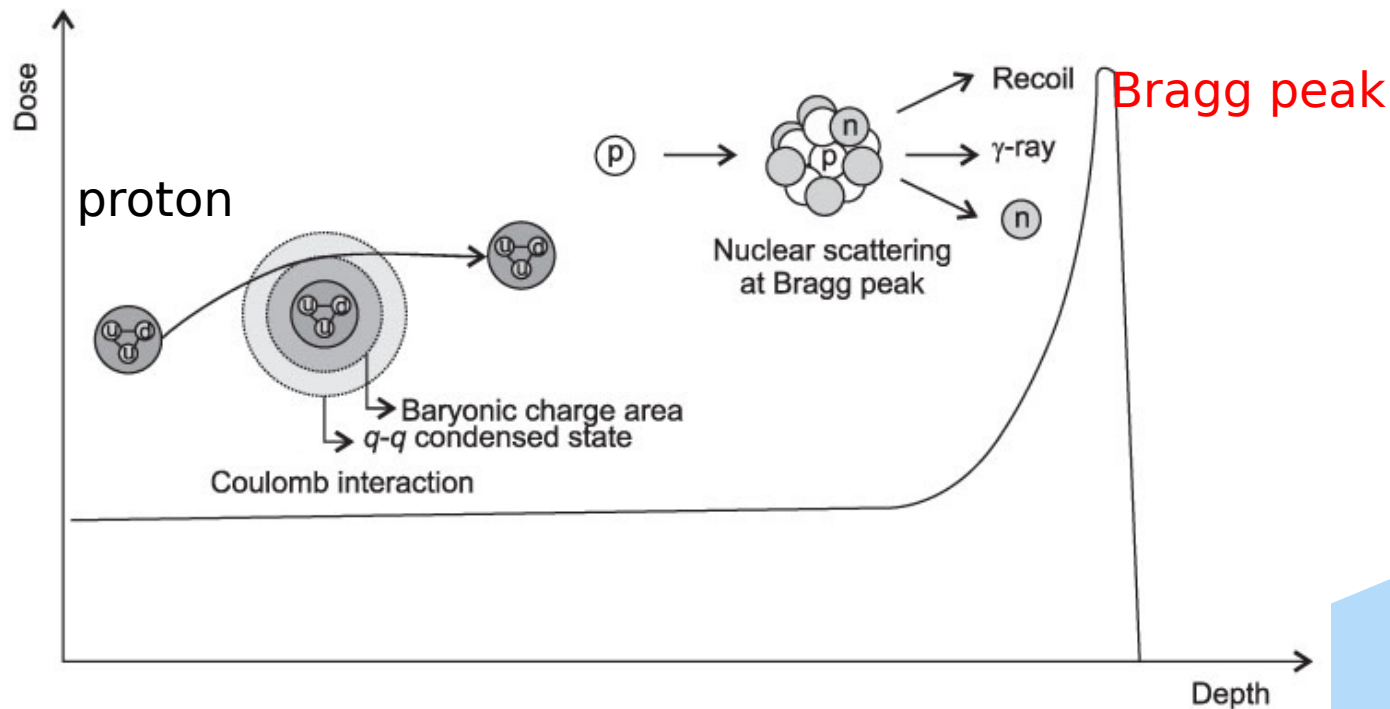# Charged particle interactions

- Energy loss through ionization and atomic excitation:
  - Bethe-Bloch formula for dE/dx
- Multiple Coulomb scattering
- Nuclear interactions

Analytical expression:

$$-\frac{dE}{dx} = \frac{4\pi}{m_e c^2} \cdot \frac{n z^2}{\beta^2} \cdot \left(\frac{e^2}{4\pi\varepsilon_0} \right)^2 \cdot \left[\ln\left(\frac{2 m_e c^2 \beta^2}{I \cdot (1-\beta^2)} \right) - \beta^2 \right]$$
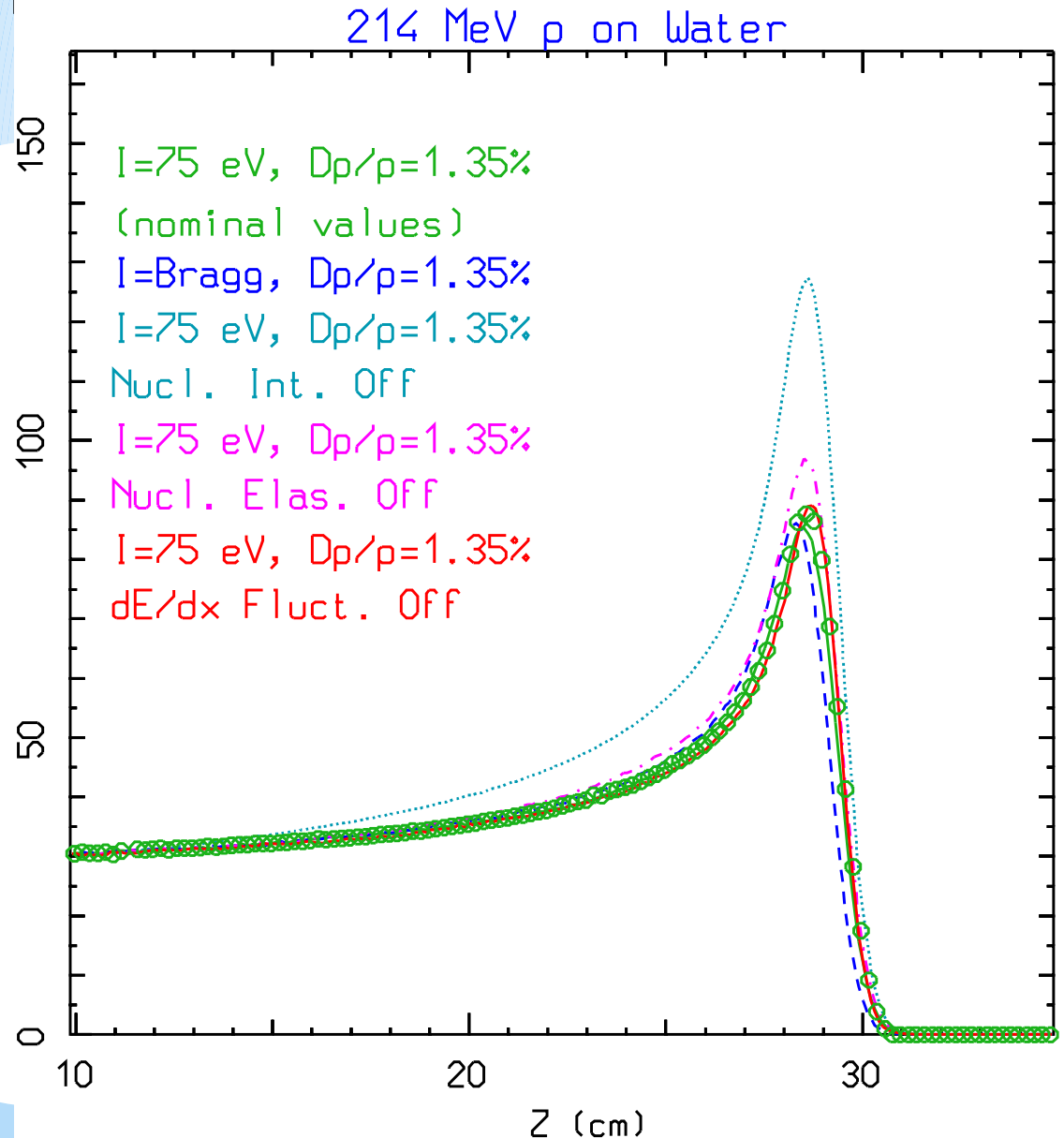
Bragg peak

proton

Recoil

γ-ray

n

Nuclear scattering
at Bragg peak

p

n

Baryonic charge area
q-q condensed state

Coulomb interaction

Dose

Depth

FLUKA: electromagnetic interactions

Proton beam:

Dose vs depth energy deposition in water for a 214 MeV real p beam under various conditions.

Exp. Data from PSI

214 MeV p on Water

I=75 eV, Dp/p=1.35%
(nominal values)
I=Bragg, Dp/p=1.35%
I=75 eV, Dp/p=1.35%
Nucl. Int. Off
I=75 eV, Dp/p=1.35%
Nucl. Elas. Off
I=75 eV, Dp/p=1.35%
dE/dx Fluct. Off

Z (cm)

Courtesy of G.

FLUKA: nuclear interactions

Ingredient in nuclear interactions:
Cross sections

Example of FLUKA prediction with experimental data
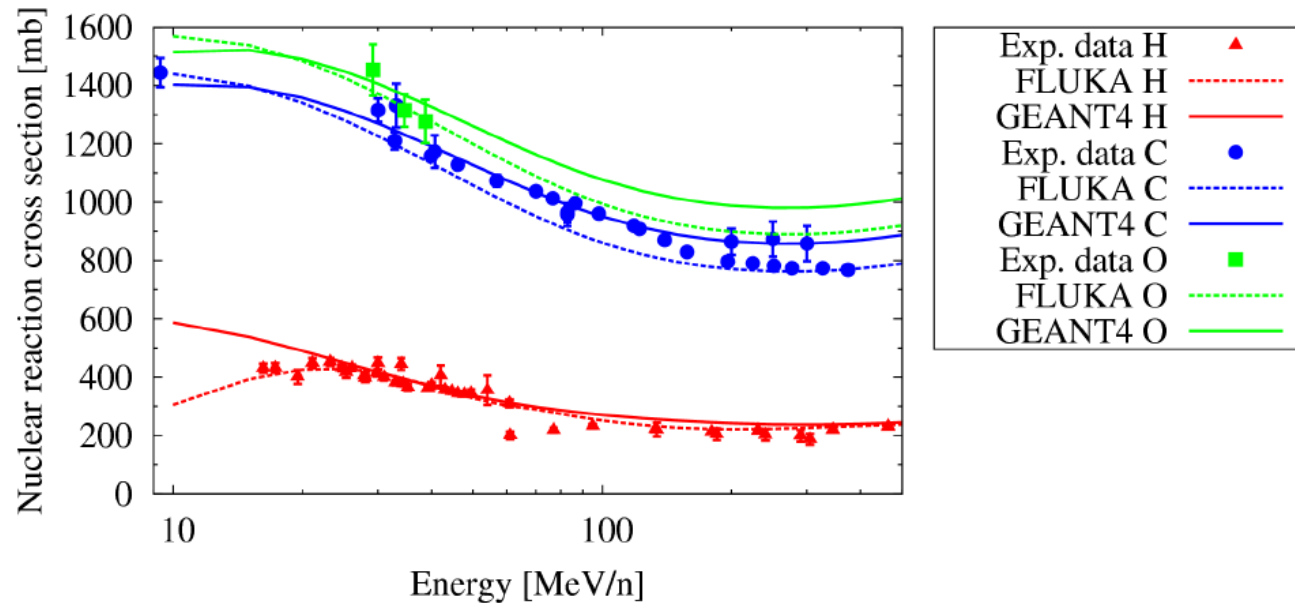
Figure 1. Total nuclear reaction cross sections for carbon ions interacting with hydrogen, carbon and oxygen are shown as predicted by FLUKA and GEANT4 together with experimental data (Fang *et al* 2000, Kox *et al* 1984, 1987; Sihver *et al* 1993, Takechi *et al* 2009, Zhang *et al* 2002).
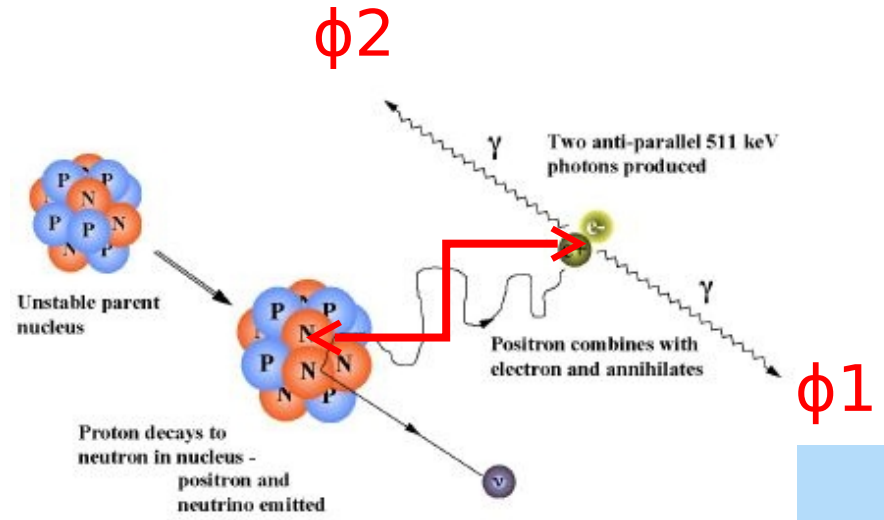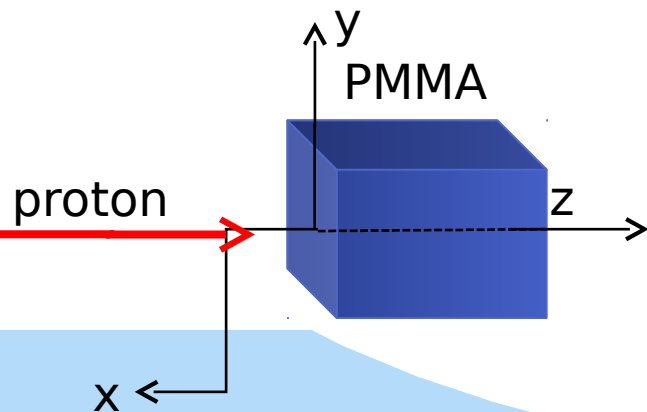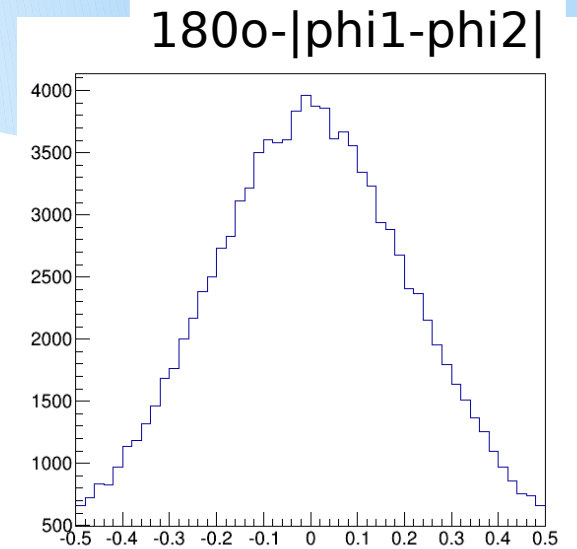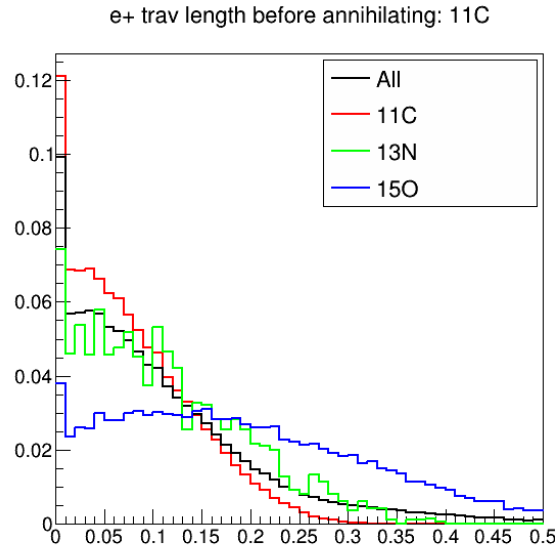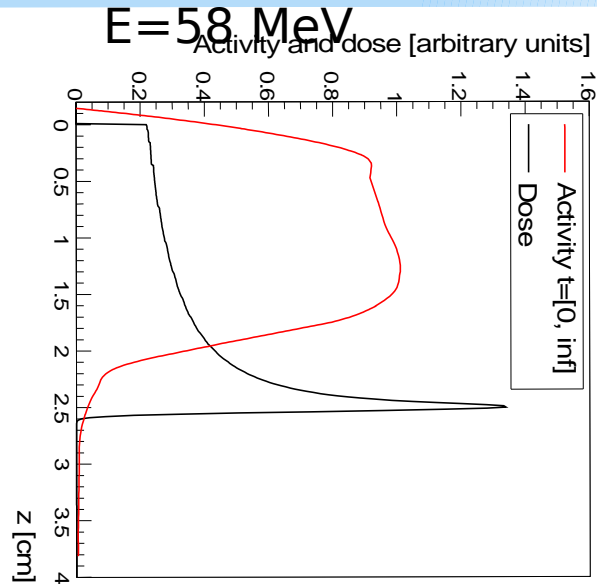
FLUKA: photon production
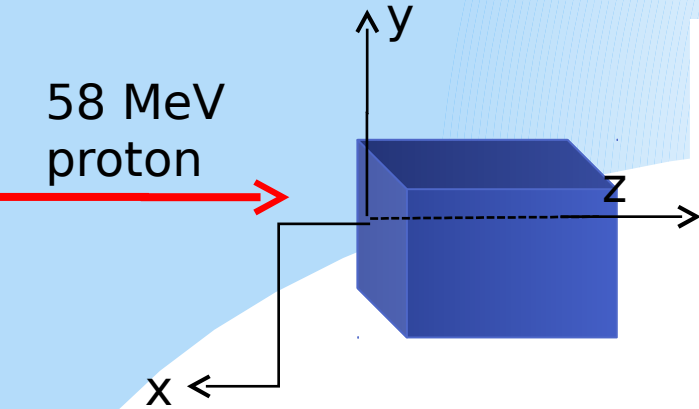
Energy spectrum of "photons" for 160 MeV p on PMMA.

FLUKA red line

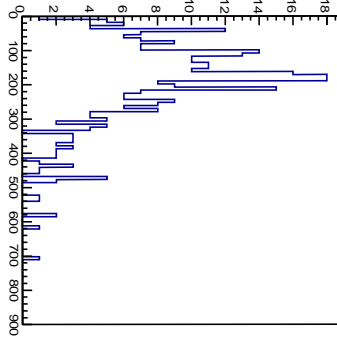Data black dots (C.Agodi et al., JINST 2012)

Prompt gamma spectra
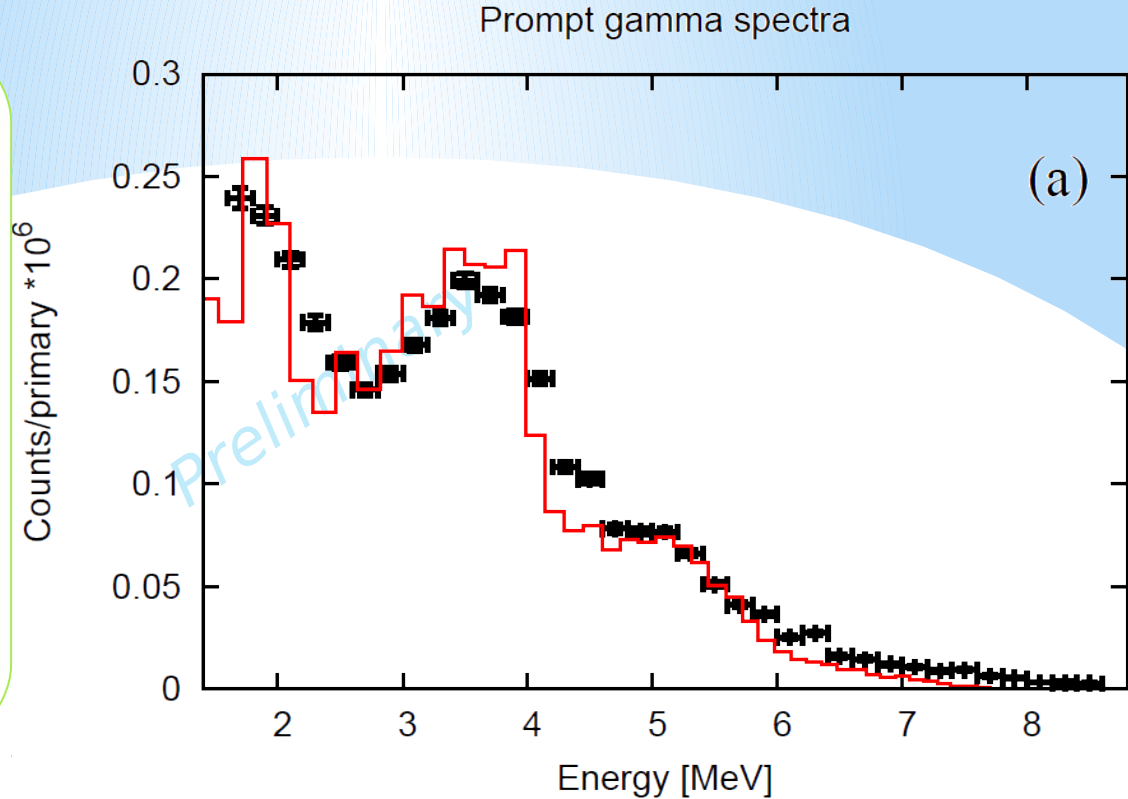
FLUKA β+ activity modeling

FLUKA β+ activity: in time
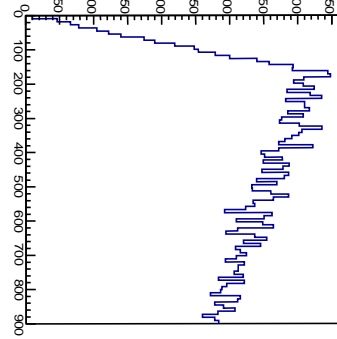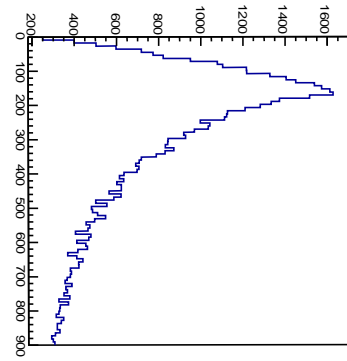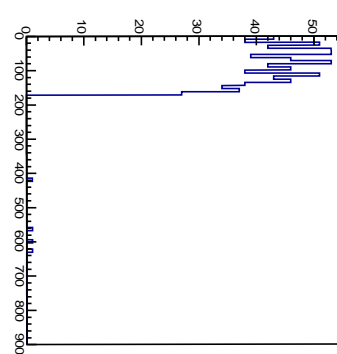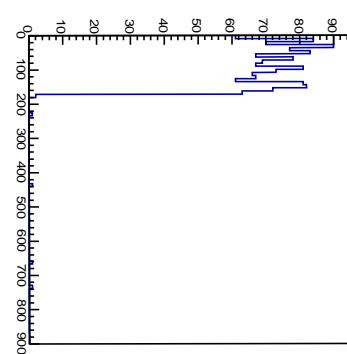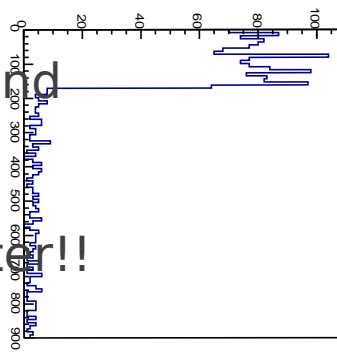
58 MeV
proton

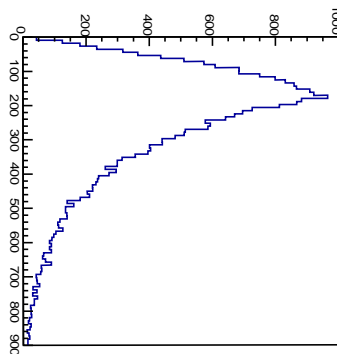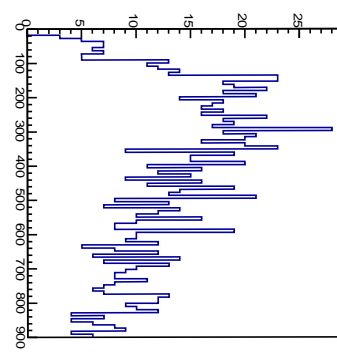- 3 minutes of proton irradiation

- Production: rise

- Decay: exponential fall

- Different shapes for long and short-lived isotopes

Comparison with data see later!!

In-beam vs after-beam

We should measure the activity as soon as possible

- to avoid patient moving
- to avoid signal to get smaller
  - physics: exponential decrease
  - biology: biological washout

☐In-beam= during irradiation

☐After-beam= after irradiation

In-beam measurements are difficult due to beam backgrounds, but important!

After-beam

In-beam

14 O: tau=71 s
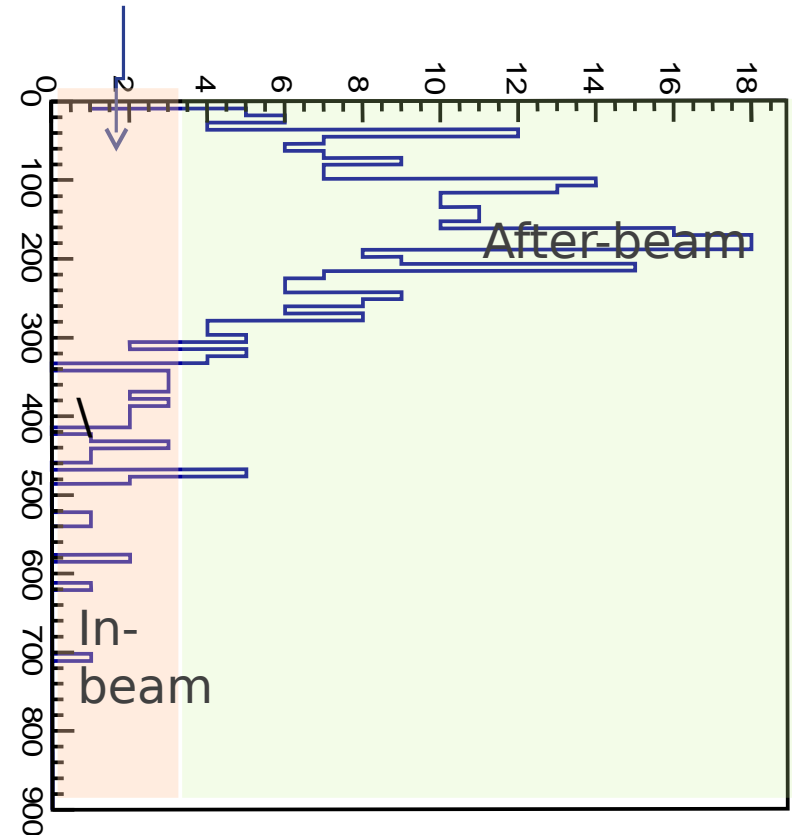
Example of ***in-beam*** 1-D z-profiles

We can check the contributions from the different Isotopes

For PMMA, main contributions are 11C and 15O.

Data taking

- Introduction: what is hadron therapy?
- Positron Emission Tomography
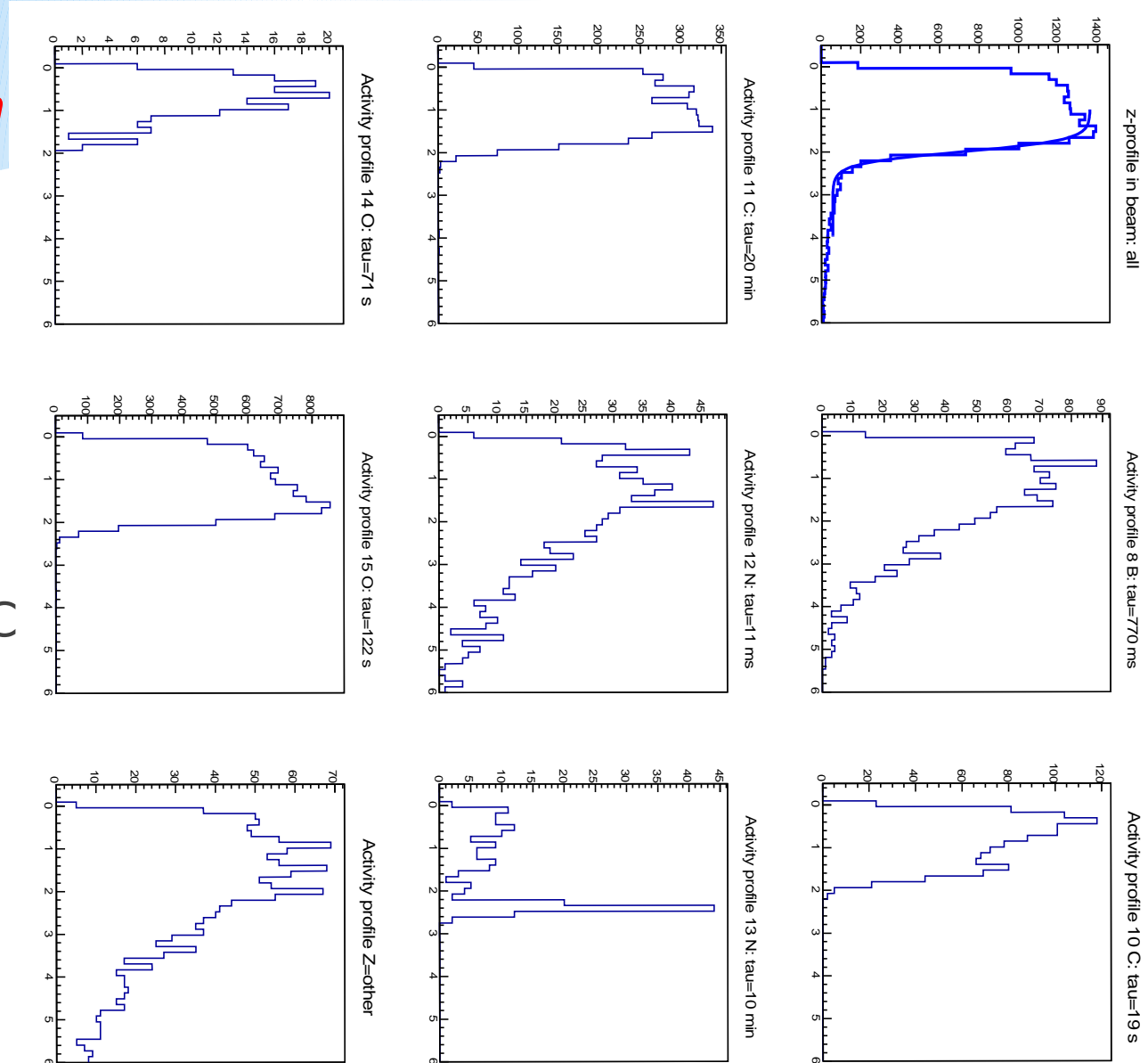- Monte Carlo simulations in hadron therapy
- Data taking: CATANA and CNAO
- Conclusion

Proton therapy in Italy

- Where do we get the protons from???
  - CATANA: **Centro di AdroTerapia e Applicazioni Nucleari Avanzate**
    - **The First Italian Protontherapy Center for the ocular melanoma treatment**
    - **Part of INFN-Laboratori Nazionali del Sud (LSN)**
    - **Proton energy: 58 MeV (Bragg peak at 2.5 cm)**
    - **From cyclotron**
    - **Beam diameter: ~3 cm**
  - Fondazione CNAO: Centro Nazionale di Adroterapia Oncologica
    - Treatment of various tumours
    - Proton energies of 50-250 MeV
    - Pencil beams (very narrow): FWHM= 1.33 cm
    - From synchrotron

CATANA

Patient treatment

http://www.lns.infn.it/CATANA/CATANA/default.htm
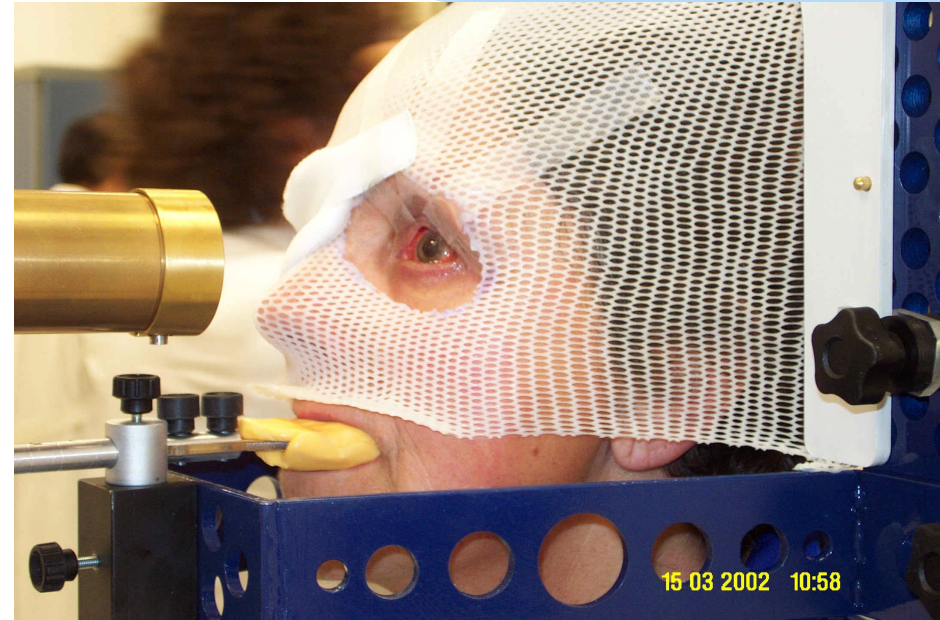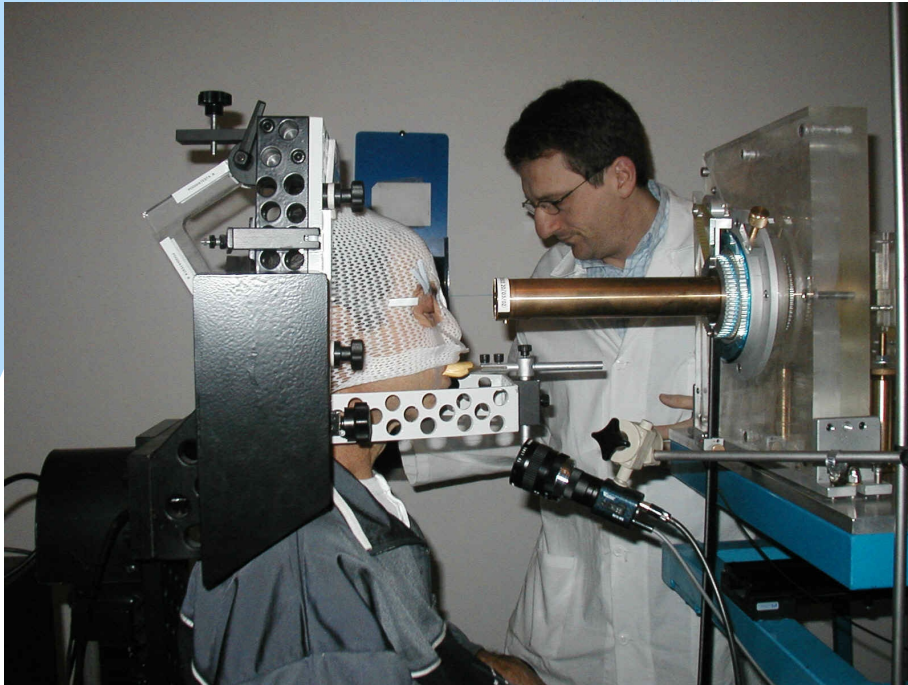
CNAO

The accelerator
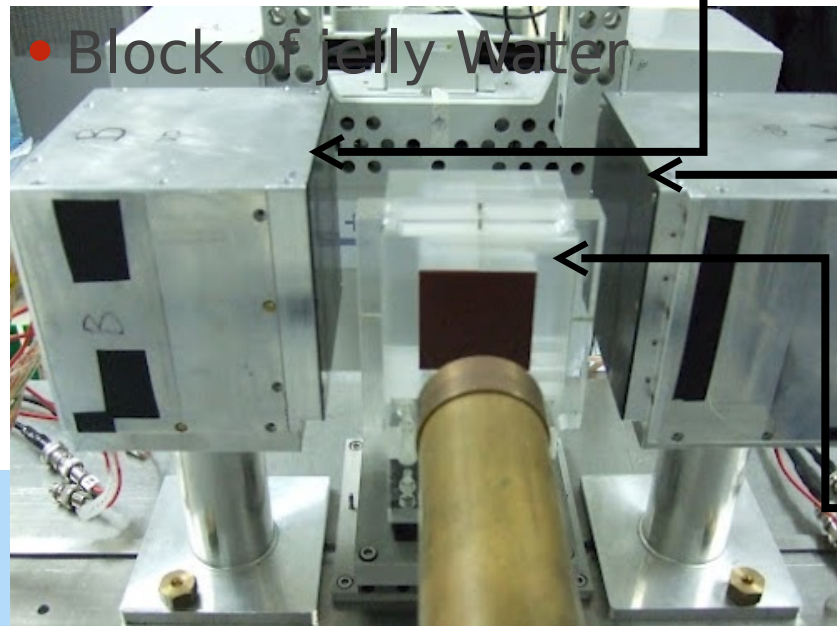
Patient treatment

http://www.cnao.it

Our measurements

Before we can work with real patients, we first must check whether the MC code predicts the activity correctly in simple materials...

Instead, our patients are:

- Block of PMMA (plexiglas)

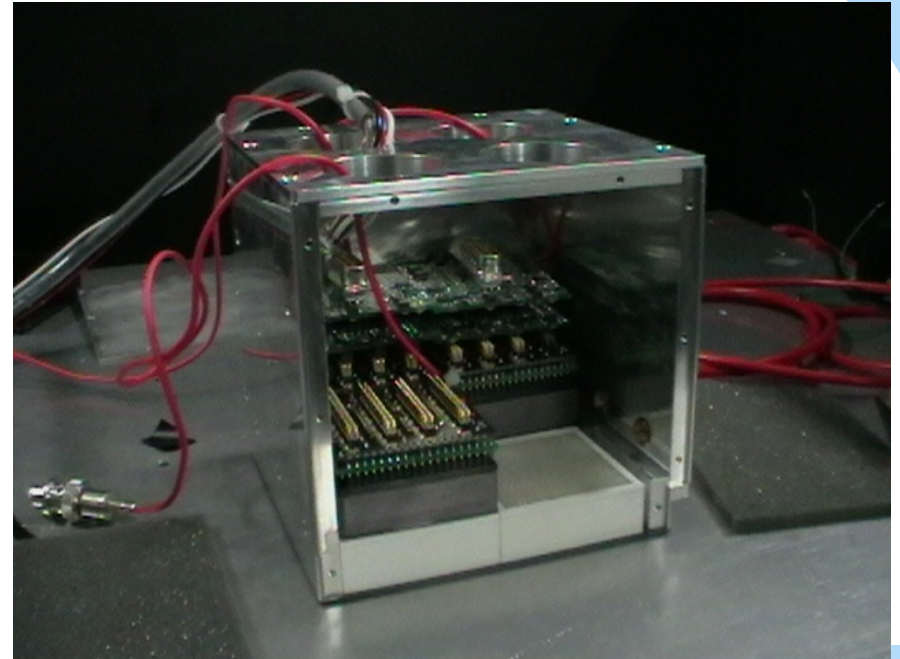- Block of Carbon

- Block of Jelly Water

PET detector

Block of PMMA

The Pisa PET-system

How do we measure the PET beta+ activity?

In Pisa (INFN, Università), we have developed a PET system which can do both in-beam and after-beam measurement

The Pisa PET-system

The motherboard with four plugged DAQ boards
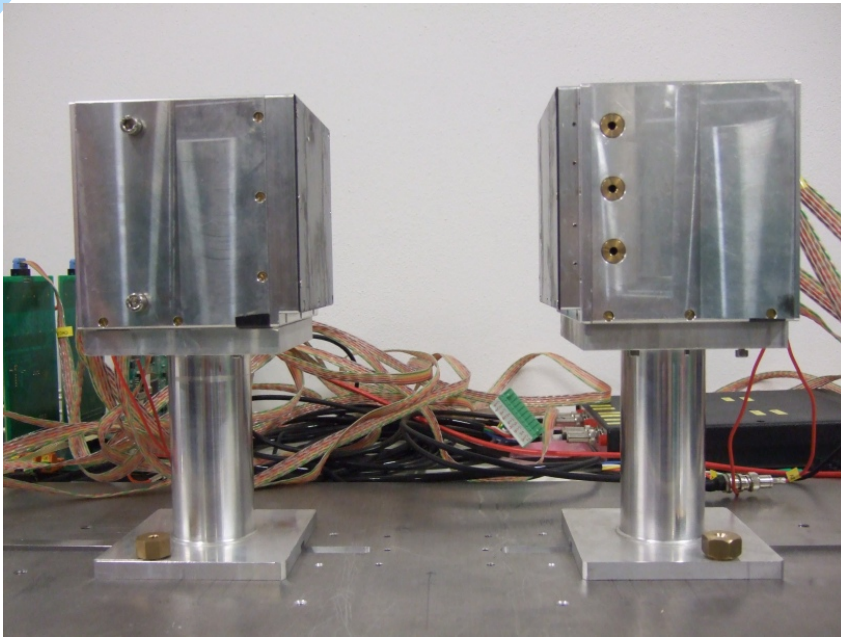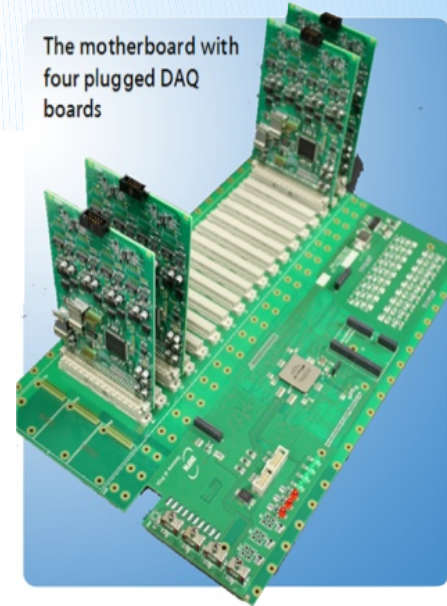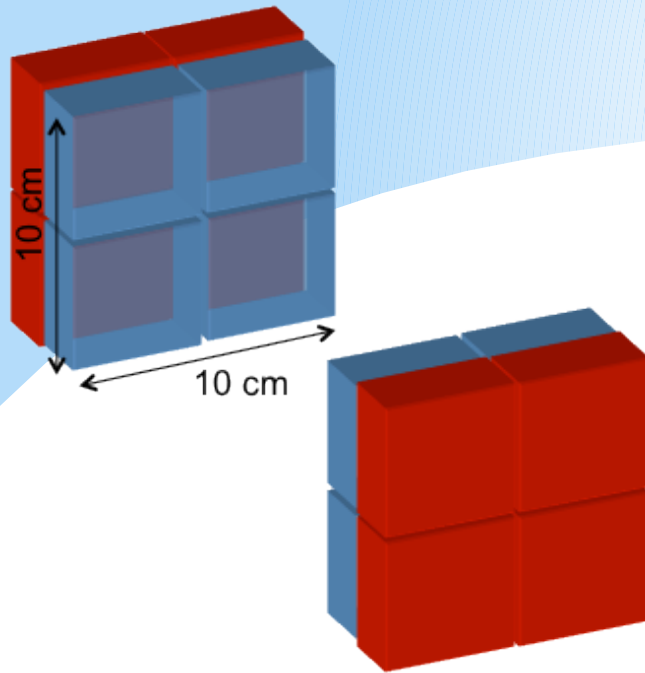
10 cm

10 cm

- Two heads, 14 cm apart
- Active area 10 cm x 10 cm, 14 cm apart
- Each head contains 4 modules
- Position sensitive photomultipliers
- Reconstruction algorithm
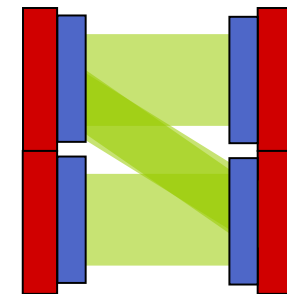
2D view of the FOV coverage of the 4+4 modules

From PET images to activity distributions

The PET system gives us PET images
extract a **time and spatial distribution for activity**

XY   XZ   YZ

XY: 5 cm, 5 cm

XZ: 2 cm, 5 cm

YZ: 5 cm, 2 cm

PMMA

proton

x   y   z
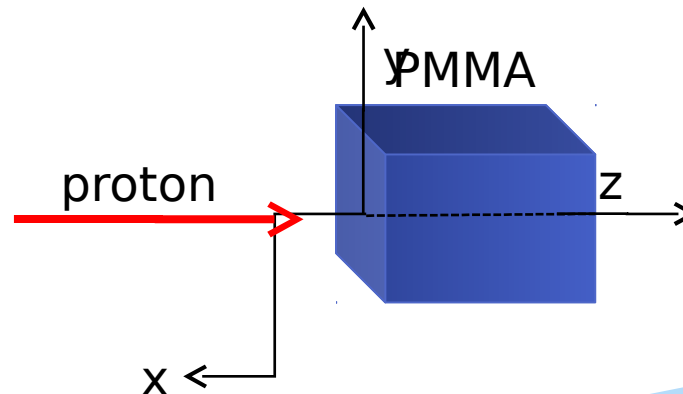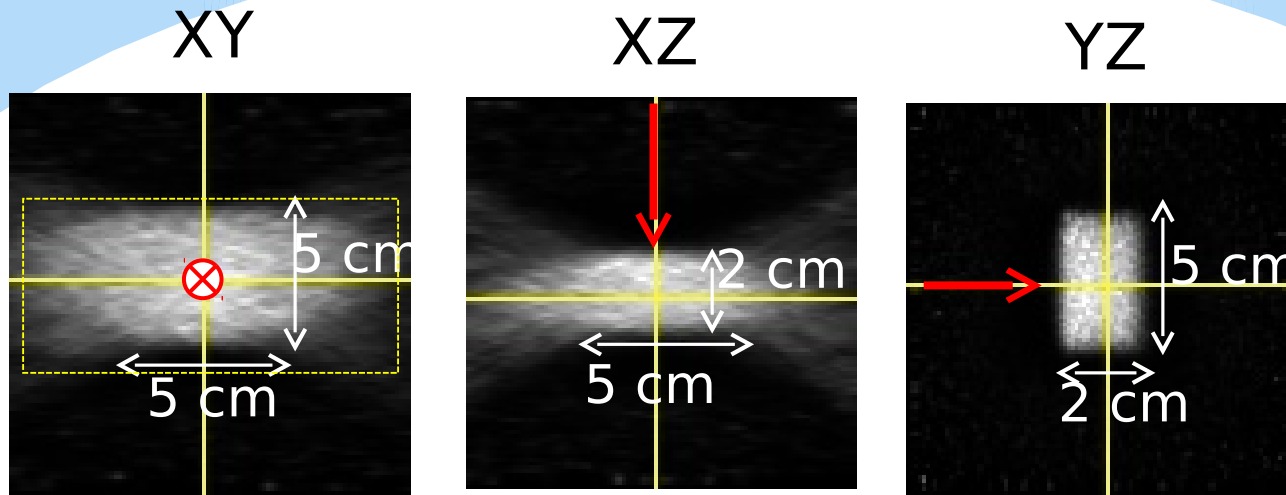
From PET images to activity distributions

Example of a time-distributions of the activity for 3 minutes or irradiation

- Monte Carlo and data aren't quite the same!
  - FLUKA not right? Nuclear cross sections not right?
  - Data not right? Problem in reconstruction? Counts not registered correctly?
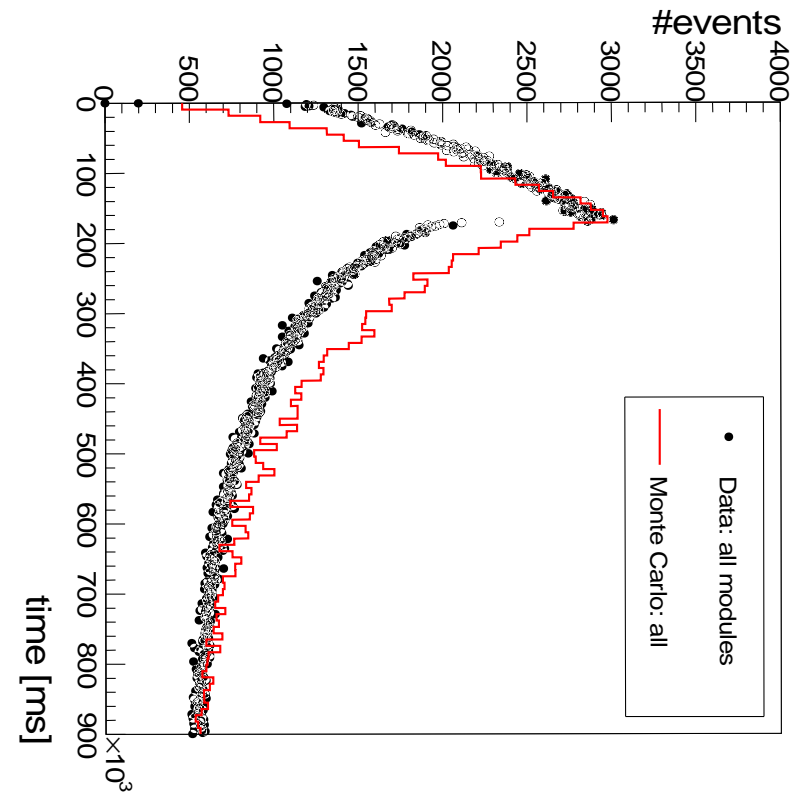
From PET images to activity distributions

Example of the spatial activity distribution: 1-D profile along the z-axis
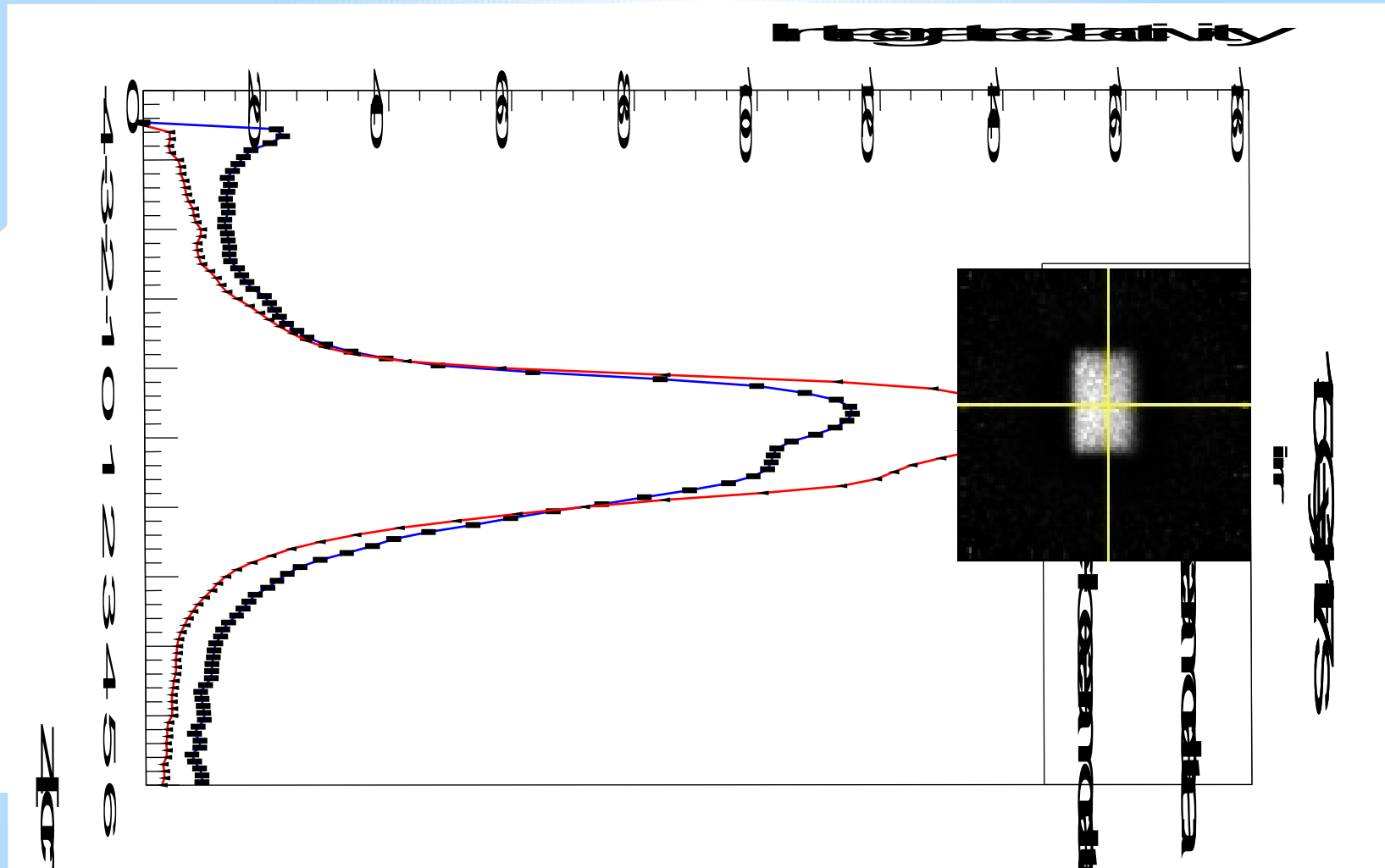
Data versus Monte Carlo: PMMA

- Shape isn't quite the same...
  - FLUKA not right? Nuclear cross sections not right?
  - Data not right? Problem in reconstruction?
- We are still validating the Monte Carlo beta+ activity model
  - More measurements for different materials
  - More measurements for different times (in-beam, after-beam)
- Only when the MC prediction and data are corresponding well, we can start to apply it to real patients

Long-term effects

Monte Carlo is also extremely important to investigate long term effects to health
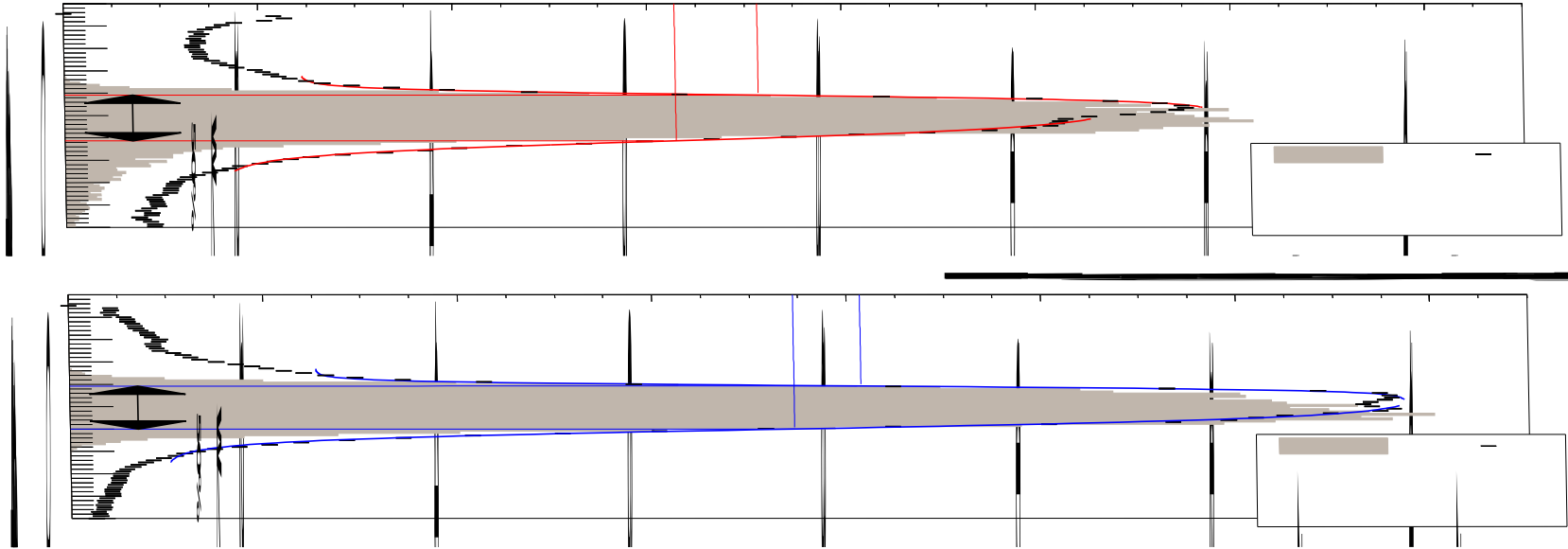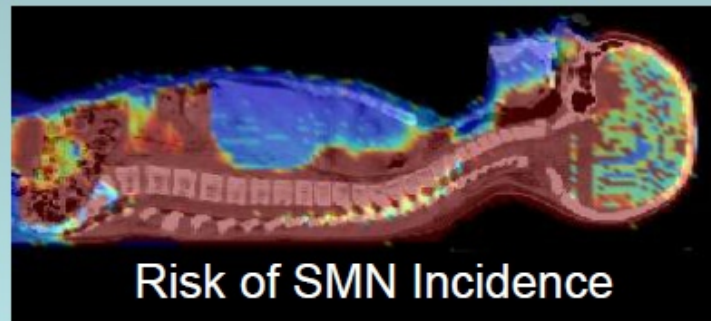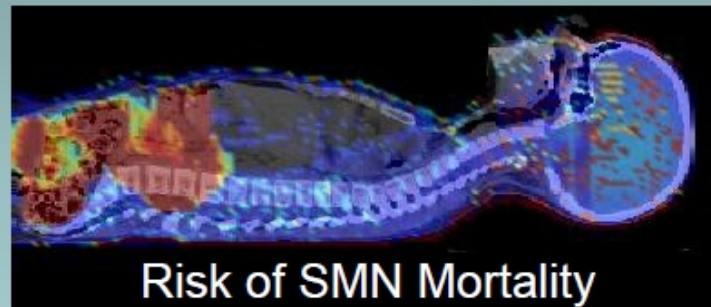
Important Issue ▯ Secondary Neutrons...

Radiation Absorbed Dose

Risk of SMN Mortality

Risk of SMN Incidence
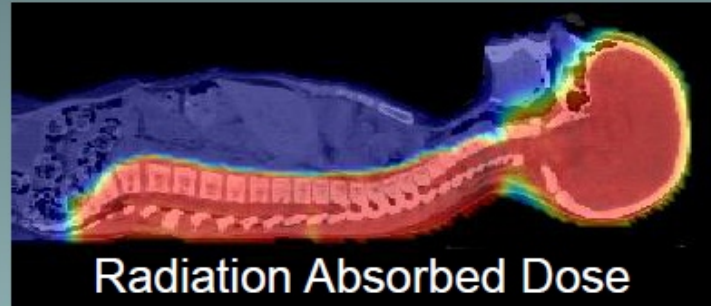
Secondary Malignant Neoplasms (SMN) in particle therapy

Comparison of relative radiation dose distribution with the corresponding relative risk distribution for radiogenic second cancer incidence and mortality. This 9-year old girl received craniospinal irradiation for medulloblastoma using passively scattered proton beams. The color scale illustrates the difference for absorbed dose, incidence and mortality cancer risk in different organs.

Newhauser and Durante, Nature Rev. Cancer 2011

FAIR

Conclusions

- Monte Carlo simulations play an important role in medical physics

- Today you saw an example of an application in hadron-therapy: proton range/dose monitoring

- Monte Carlo generators are predicting very well quantities like energy and dose deposition, nuclear cross sections, etc.

- Still, the beta+ activity is not yet perfectly predicted in FLUKA (problem can be in data or in MC).

- At INFN/Università di Pisa, we are working on the development of an in-beam proton range monitoring system, which eventually will be applied to patient treatments

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*Spec's of hadrontherapy monitor

Origin of highly penetrable signals: nuclear processes

Projectile → Projectile fragment → Nucleons and clusters → Radioactive nuclides

Fireball

Target — Target fragment

Prompt γ-rays
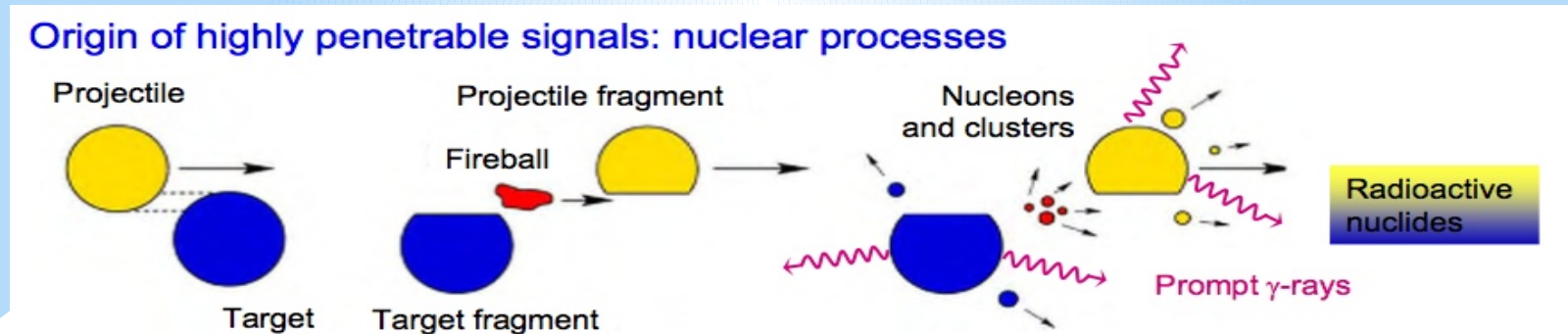
*Measure shape and absolute value of dose to check the agreement between the planned target volume and the actually irradiated volume

*The measurement should be done during the treatment (in-beam)

*Must rely on a given secondaries generated by the beam that comes out from the patient, to spot the position of the dose release

*Must be able to deal with the other secondaries that come out that acts like background

*baseline dose monitoring in HT : PET

Baseline for monitor in HT is PET : autoactivation by p & 12C beam that creates β+ emitters.

* Isotopes of short lifetime 11C (20 min), 15O (2 min), 10C (20 s) with respect to conventional PET (hours)

* Low activity in comparison to conventional PET need quite long acquisition time (few minutes)

* Metabolic wash-out, the β+ emitters are blurred by the patient metabolism

* No direct space correlation between β+ activity and dose release (but can be reliable computed by MC)

Energy and dose

area **A**

N protons

Δ**x**
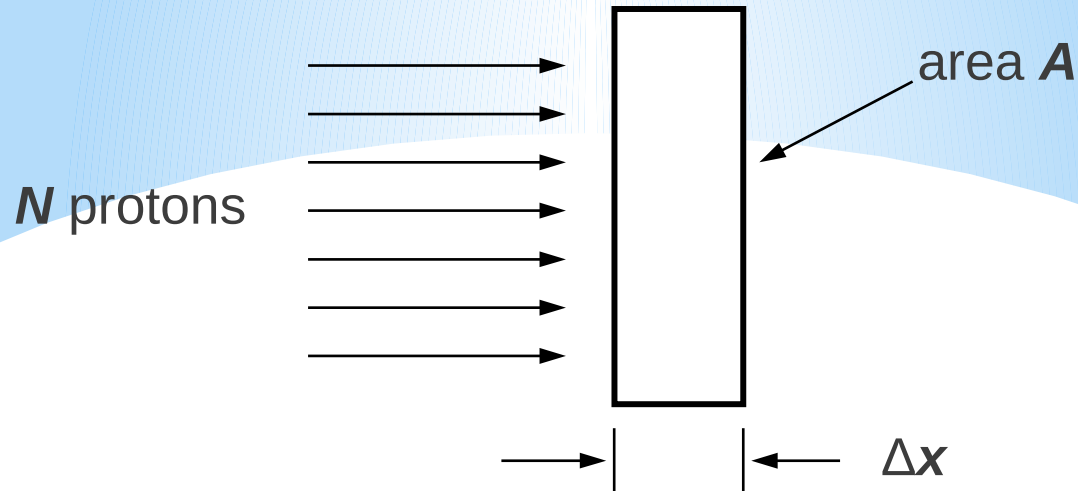
The equation relating dose to fluence and stopping power is the starting point of most beam line design problems. From the figure :

$$D \equiv \frac{\text{energy}}{\text{mass}} = \frac{(dE/dx) \times \Delta x \times N}{\rho \times A \times \Delta x} = \Phi \; \frac{S}{\rho}$$

dose = fluence × mass stopping power