The performance of scintillating fibre based beam profile monitor for ion beam therapy

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Beam-on profile detector for Heidelberg Ion Therapy (HIT)

- Proton/Helium/Carbon/Oxygen beams at different intensity / energy/ focus
- **Beam-on profile detector** is designed to support a **raster scanning dose delivery method** (Scanning magnets to change the direction of the beam)

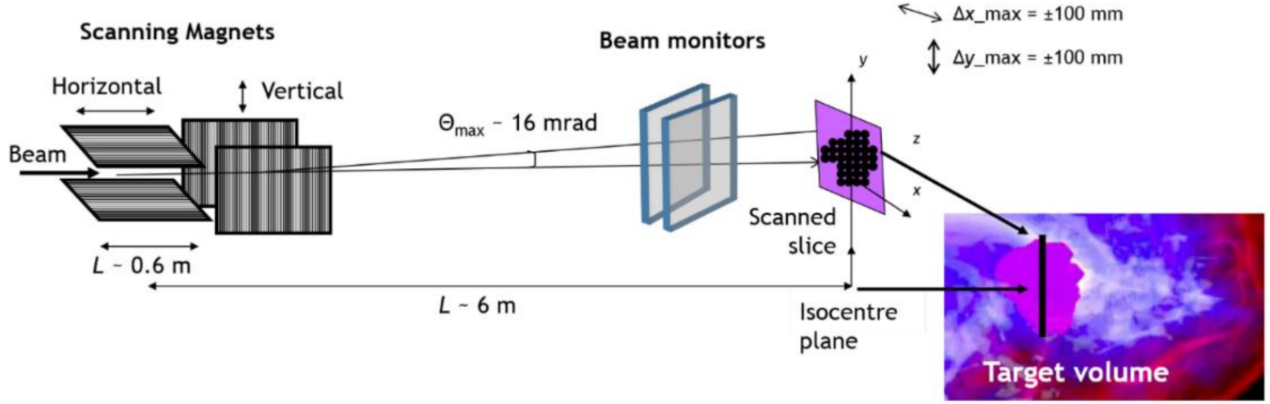
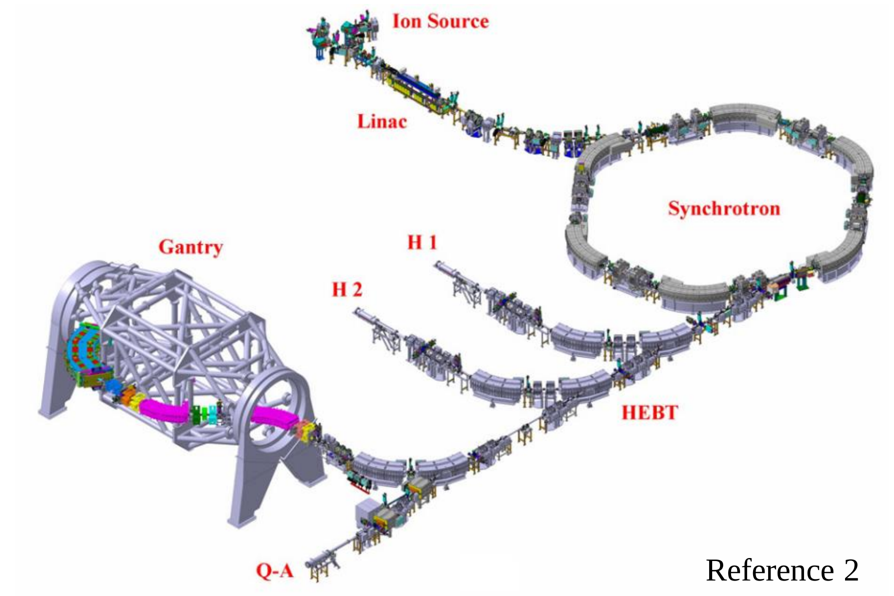
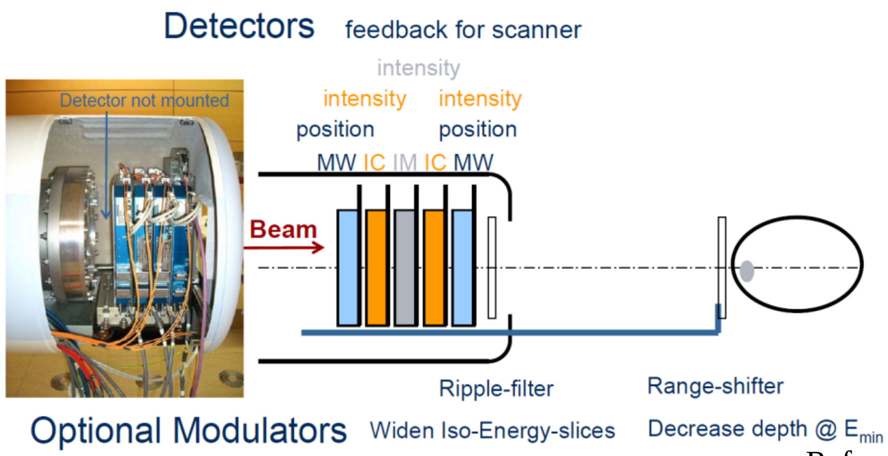


Fig. 9: Example of a fixed horizontal beamline for modulated spot scanning delivery   Reference 3



Reference 2

- Vertical and Horizontal **MWPC**(Multi-wire proportional chamber) detector to monitor the **Position** / **Focus** of the beam
- **IC**(ionization chamber)→**Intensity** of the beam

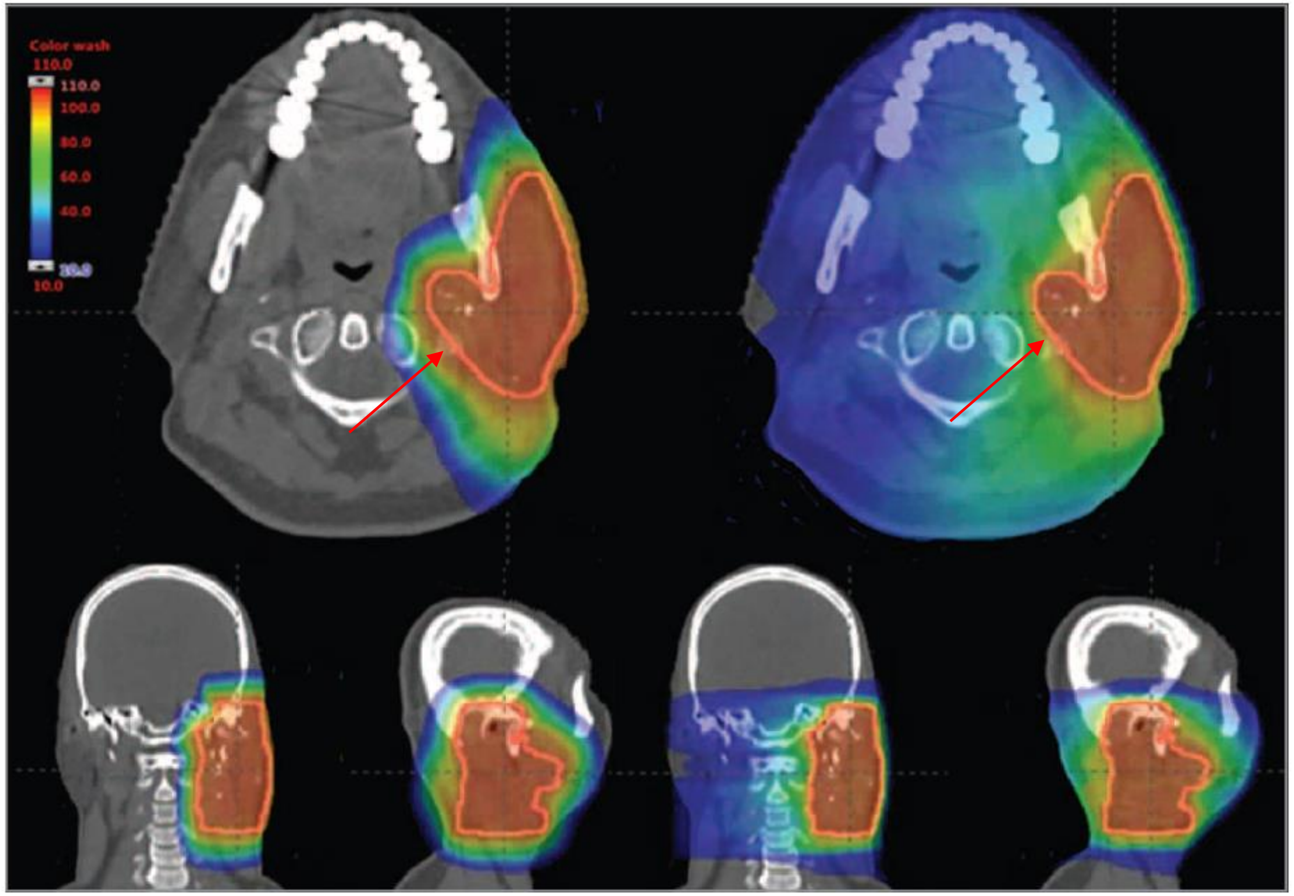


Reference 1

Why Beam on detector for raster scanning dose delivery method?

- Bragg peak → a low entrance dose increasing to a maximum beyond, which there is a sharp reduction in dose deposition
- This can give less dose to normal tissues and maximum dose to the target if the beam is on the right area!
- But if the beam is at wrong position(outside of the treatment plan) →damage the healthy tissue!
- Beam-on profile detector can give a immediate feedback to the system if the beam is on the wrong area
- It also give the profile of the beam on real time so that it can minimize the dose of the normal tissue at the edge of the tumor

Figure 1. Representative Proton and Photon Treatment Plan for a Patient With Head and Neck Cancer



Proton Therapy Photon Therapy

Reference 6

Beam profile detector

Old gas-based detectors

MWPC(Multi-wire proportional chamber)

→ limited the intensity (gas detector limit --sparking)

→ionize gas drift time ~1 ms/raster point

→ the granularity of the MWPC is limited by the **2 mm** wire spacing

→ Sensitive to magnetic field and acoustic noise

Upgrade the monitor system (~2030)

Requirement	Value
Beam Spot Size (FWHM)	1–33 mm
Beam Position Resolution	< 0.2 mm
Beam Width Resolution	< 0.4 mm
Readout Rate	4–8 kHz
Dead Time	< 250 µs
Material in Active Area	< 0.35 mm H_2O eq./plane

Four ions beam intensity : 10^6 ~ 10^{10} per second

Table 1. The energies and intensities available at the HIT Clinic. The energy range is divided into 255 possible settings, E1–E255. There are typically 10 different intensity settings available for use, I1–I10.

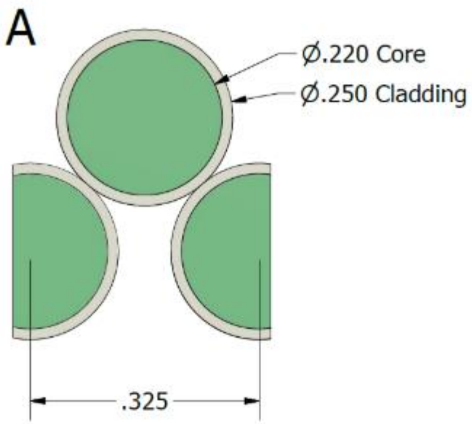
	Protons	Helium	Carbon	Oxygen
Energy [MeV/u]	48–221	51–221	89–430	104–515
Intensity [s^{-1}]	$8\cdot10^7$–$3.2\cdot10^9$	$2\cdot10^7$–$8\cdot10^8$	$2\cdot10^6$–$8\cdot10^7$	$1\cdot10^6$–$4\cdot10^7$

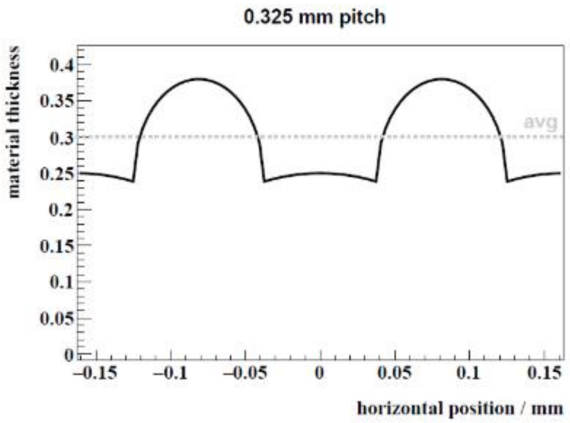
Scintillating fibre based detectors

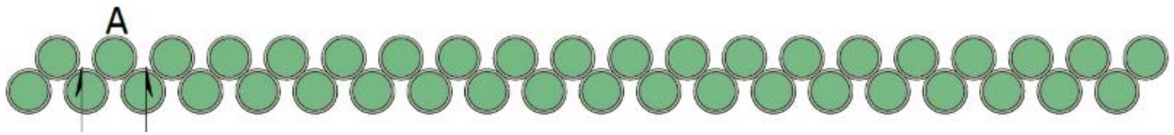
- Fibre : Kuraray green 3HF scintillating fibres

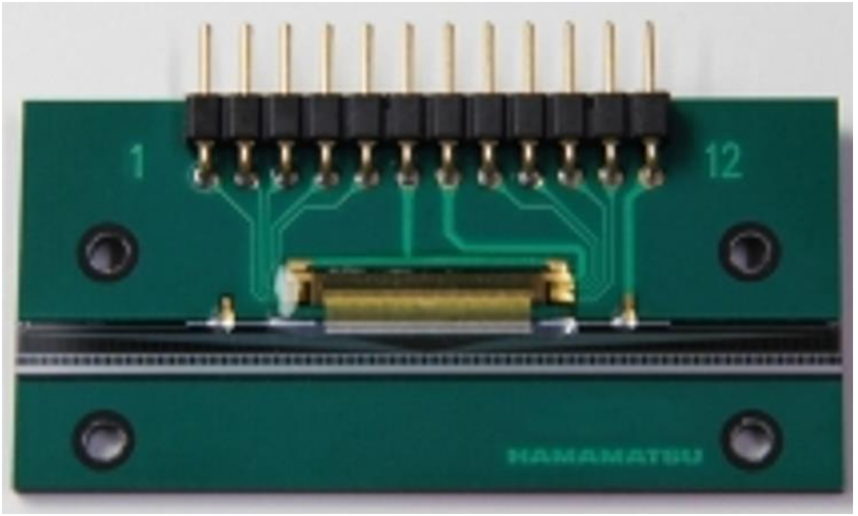
- Minimize the material: 2 layer of scintillator fibre (no epoxy 0.3 mm polyethylene have similar density with water)

- Hamamatsu S11865-64 photodiode arrays with a pitch of 0.8 mm (64 channel)









- Integration time: 100 μs-100 ms (adjustable)

The different shape of the beam

- Shape depends on energy, intensity and ion species
- Collecting photon for each 100 µs frame have statistical differences
- Beam is not perfectly stable in time; fluctuations in RF kicker beam extraction
- Shape is dependent on the momentum of the particles (multiple scattering)
- Position /focus /peak resolution is directly related to the reconstruction algorithm

Need a reliable and fast real time **reconstruction algorithm** which can be programmed in the FPGA to analyze each data frame(100 µs)

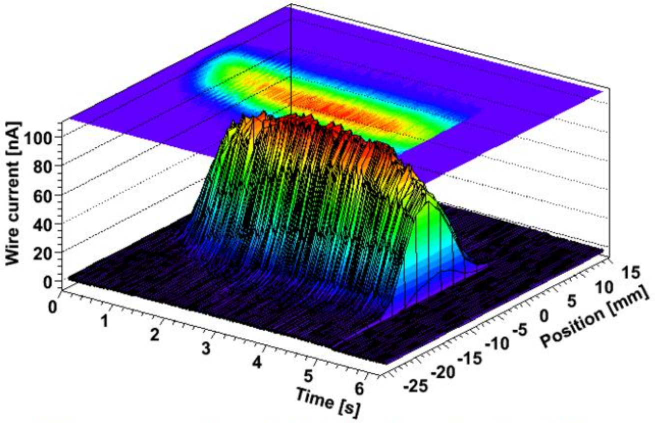
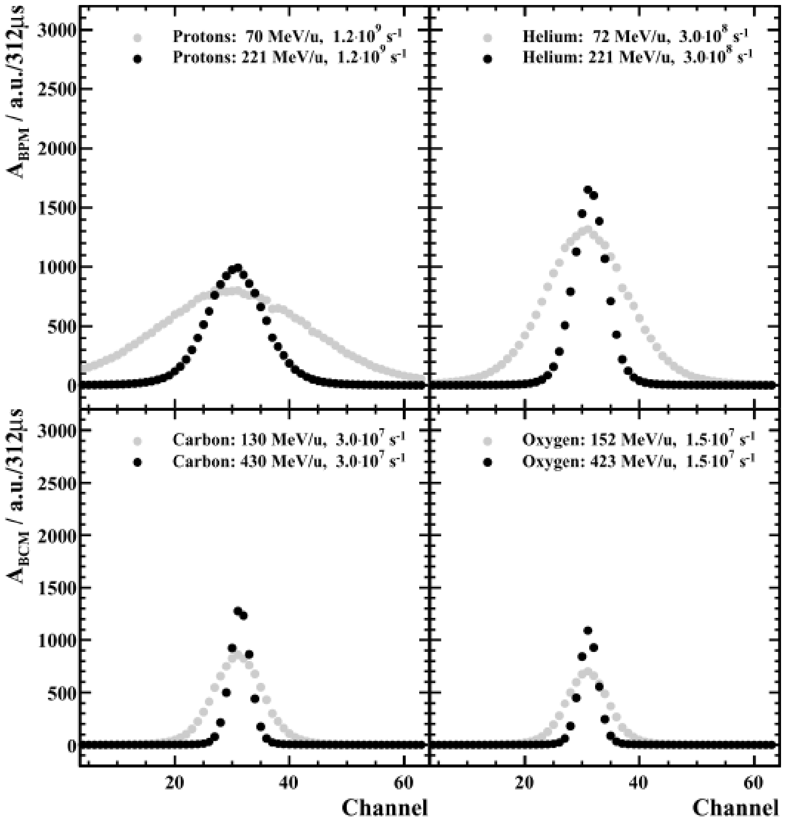


Figure 3: Horizontal distribution of a 5 s spill.

Reference 4

isocenter



Reference 5

Experimental setup

Experiment of detector with epoxy and without epoxy

4 boards are in the same direction → horizontal

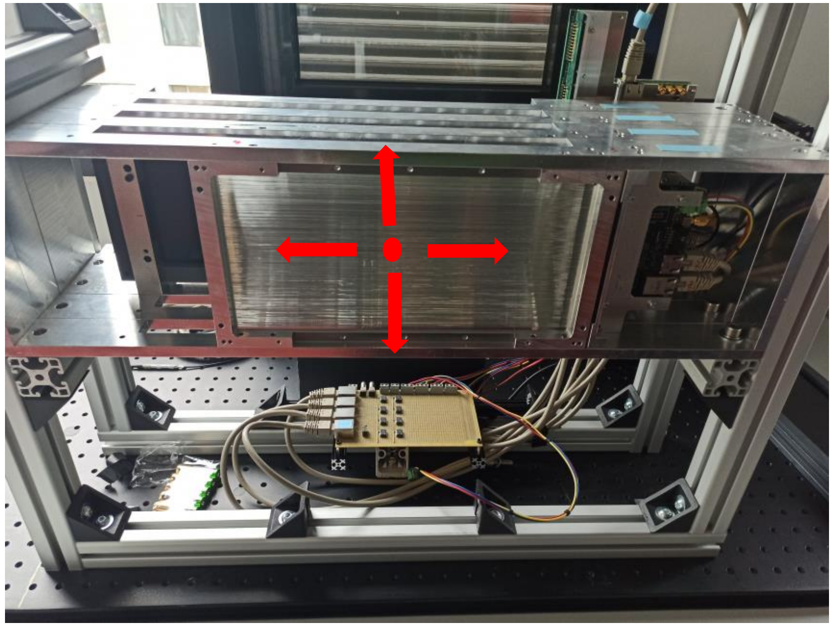
board 0 is the rear detector

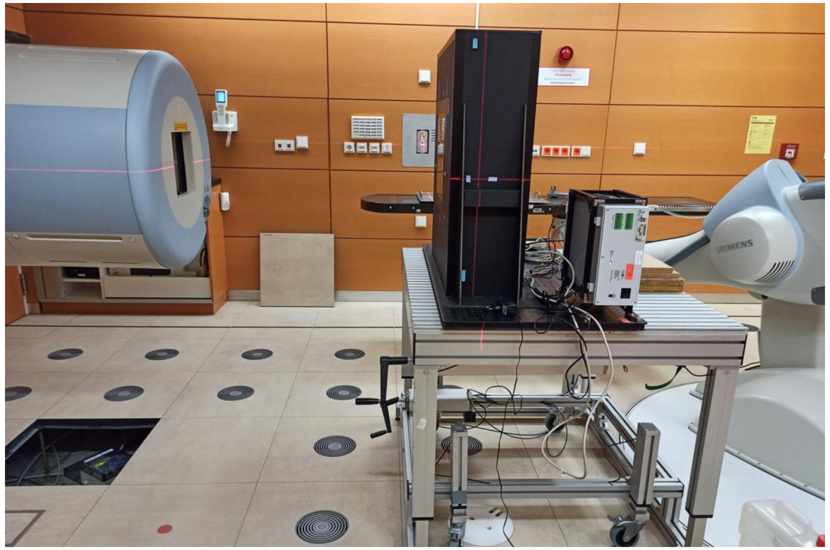
Board 0 : two layers fibre with epoxy / 400mm / no mirror at the end

Board 1 : two layers fibre with epoxy /400mm/ radiation damage / mirror

Board 2 : two layers fibre without epoxy / 300mm / mirror

Board 3 : two layers fibre without epoxy / 300mm / mirror





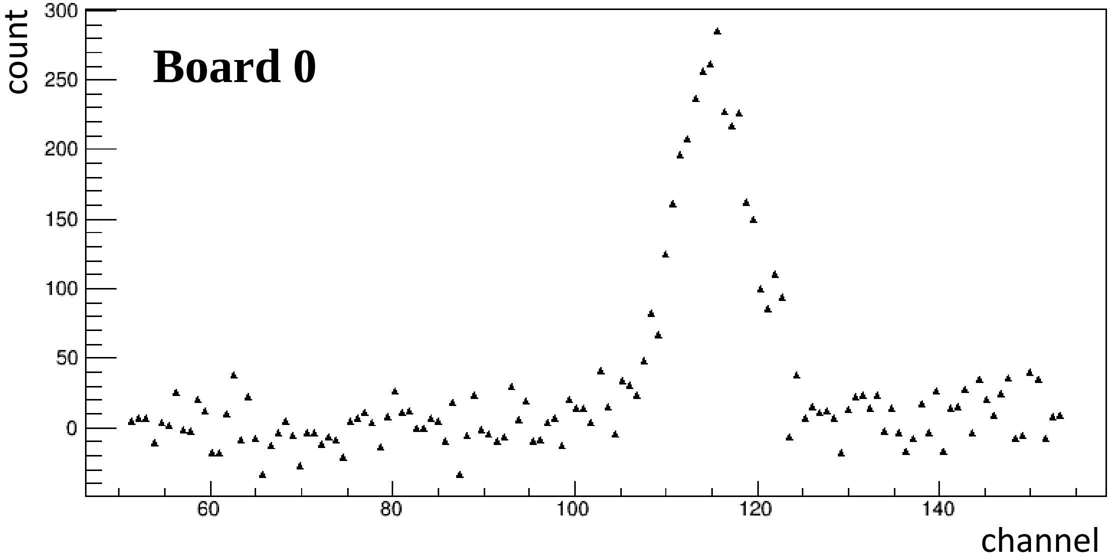
Collect the data : energy scan, intensity scan, position scan etc…….

Development History : 5 layer fibres with epoxy→ 2 layer fibres with epoxy→ 2 layer fibres without epoxy

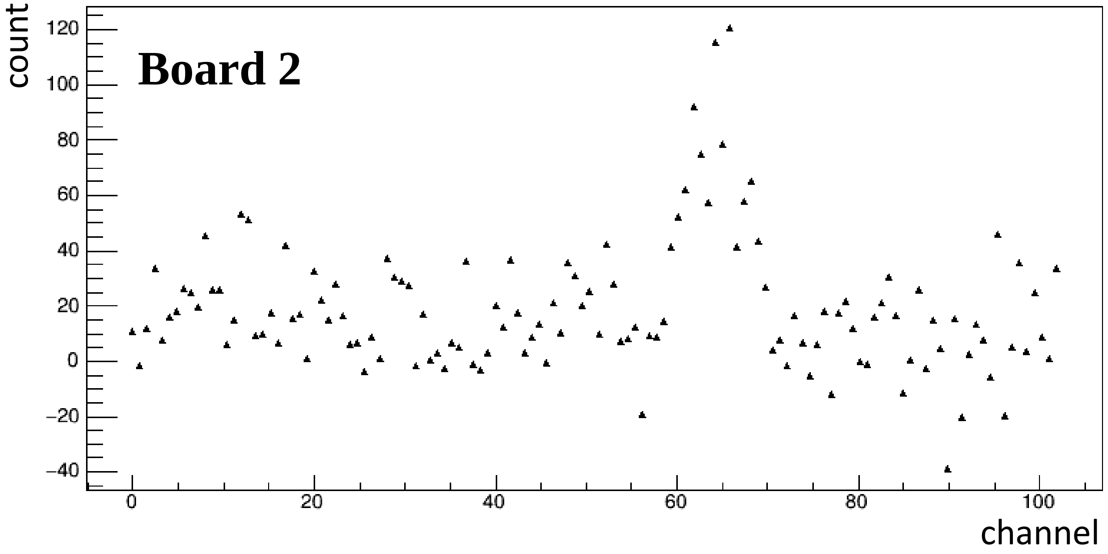
Example of frame profile

- Example of high/low intensity
- From the low intensity frame we can clearly see the systematic bias of the signal which could probably caused by light production, optical coupling, radiation damage, photosensor → need **calibration**!

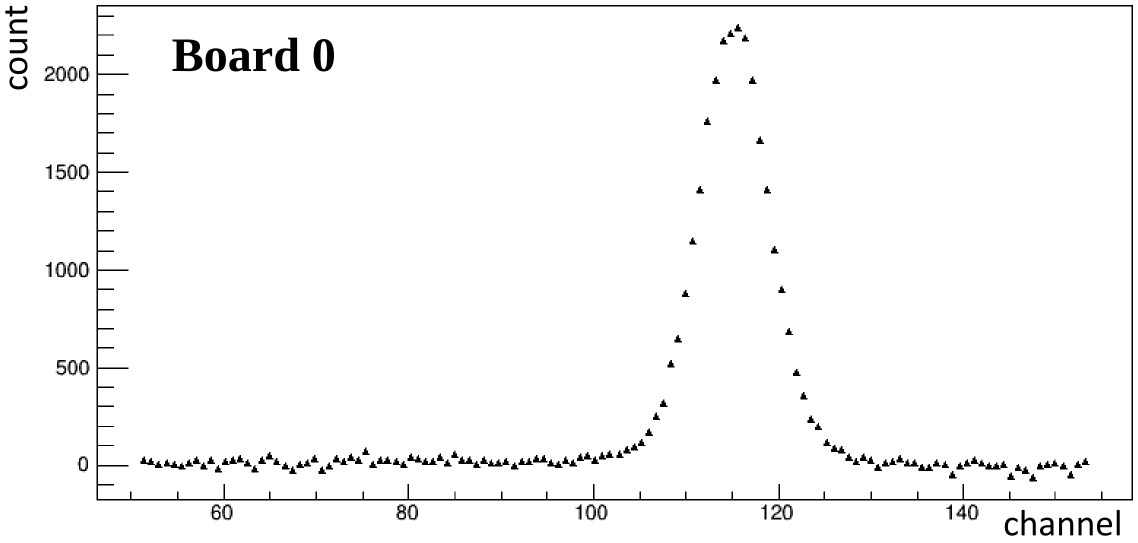
Proton: 255 MeV ; intensity 126 10^6 s^{-1}



Proton: 255 MeV ; intensity 126 10^6 s^{-1}



Proton: 255 MeV ; intensity 2322 10^6 s^{-1}

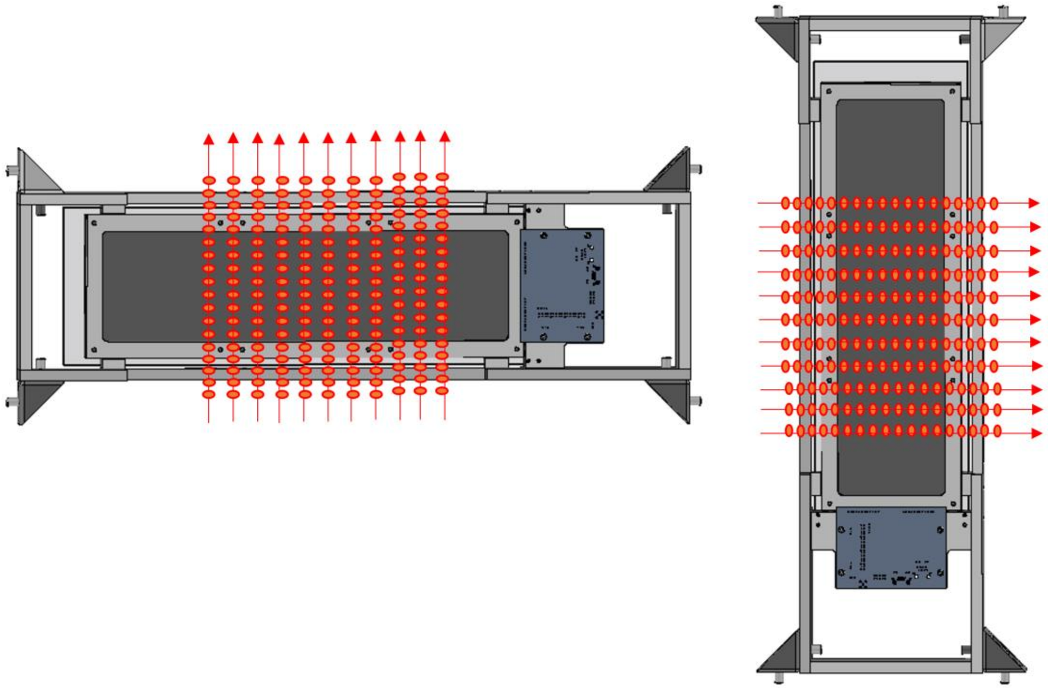


Calibration

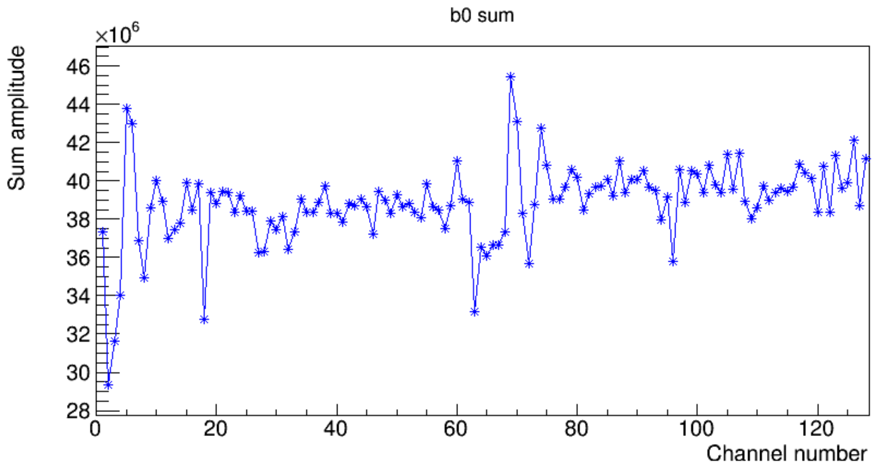
Purpose:

Calibrate the variations among channels (light production, optical coupling, radiation damage, photosensor) → systematic bias of the signal

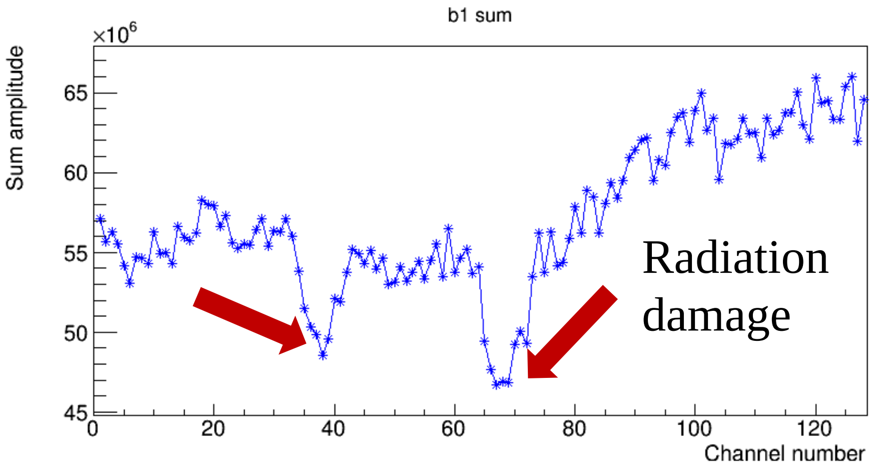
Method:
Use 2 Beam plans (XY and YX scan) →Scan the x and y direction in steps of 1 mm to get the sum of the signal to correct vertical and horizontal plan

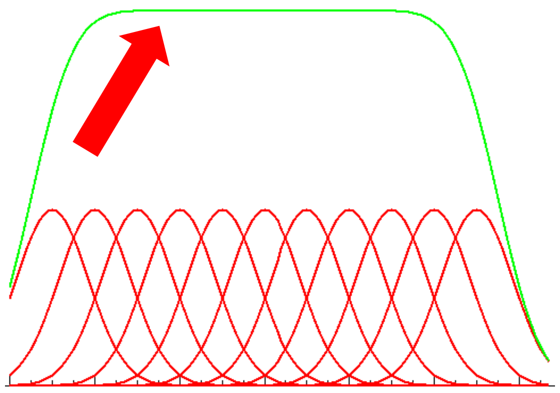


Vertical



Horizontal

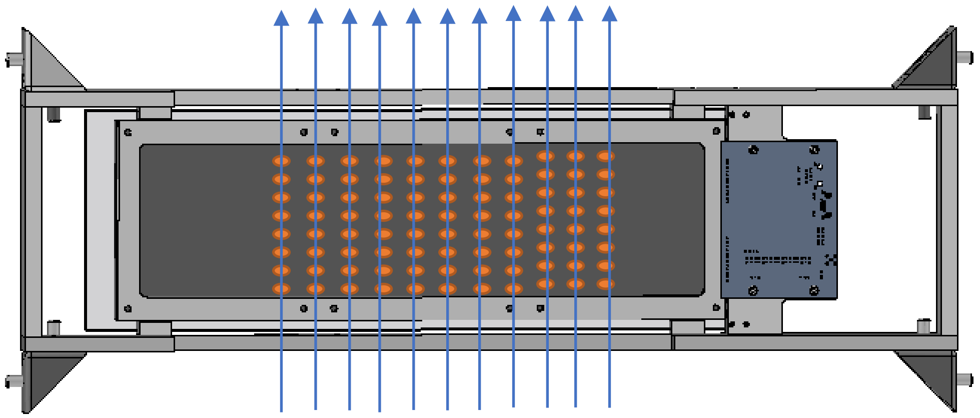




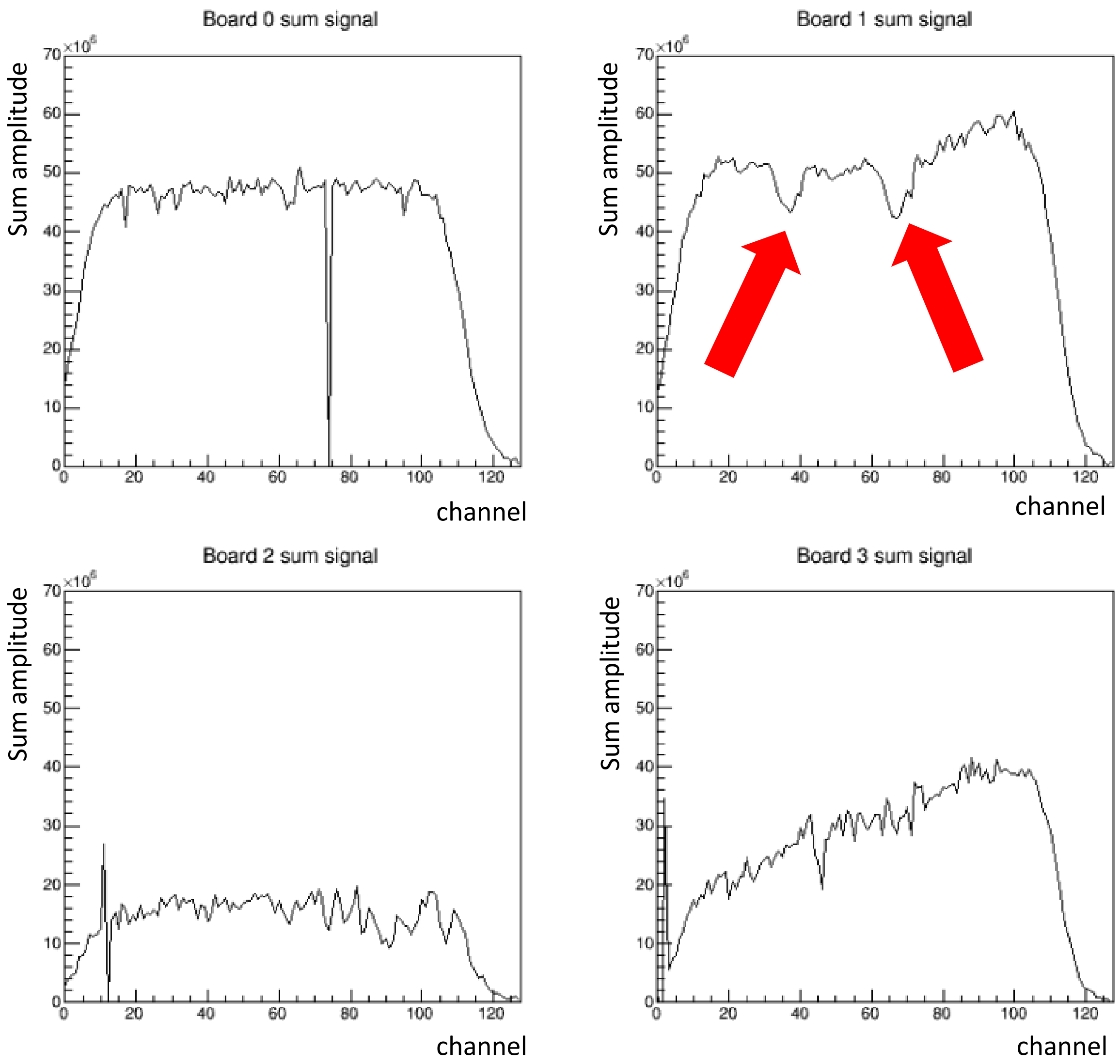
Sum of the signal

Scan across the board at different height of the fibre

Sum up the signal per each channel



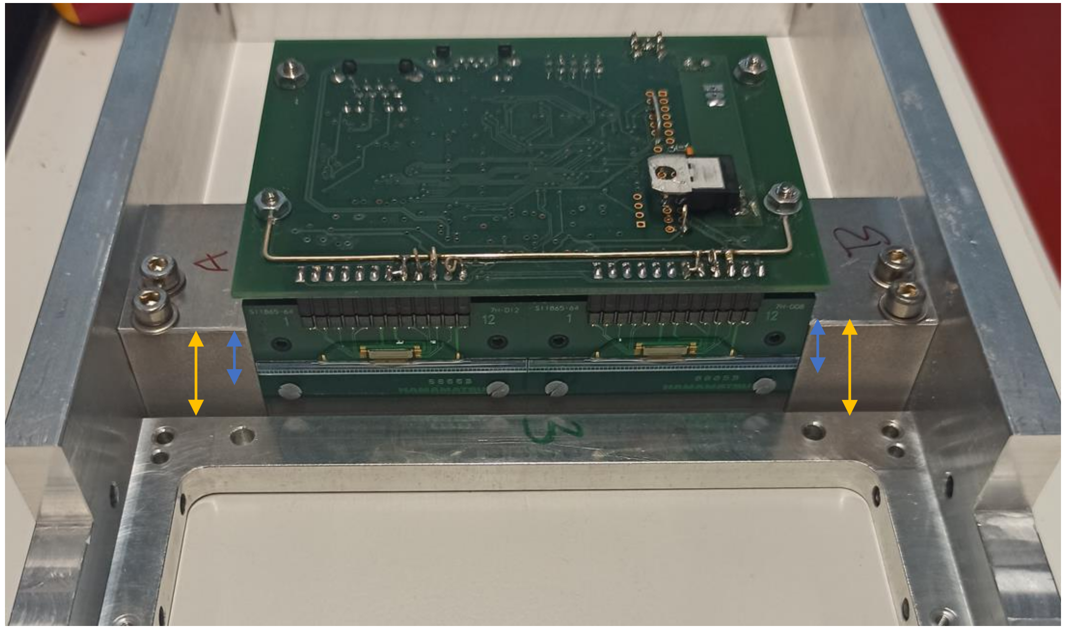
Scan at different height (10 mm interval) of the fibre mat with the beam step of 1 mm



Misalignment

Board 3

Board 2



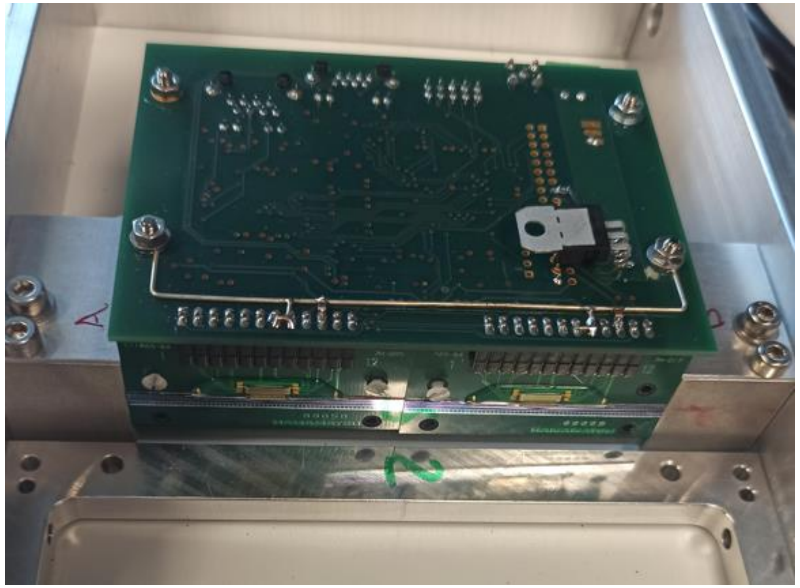
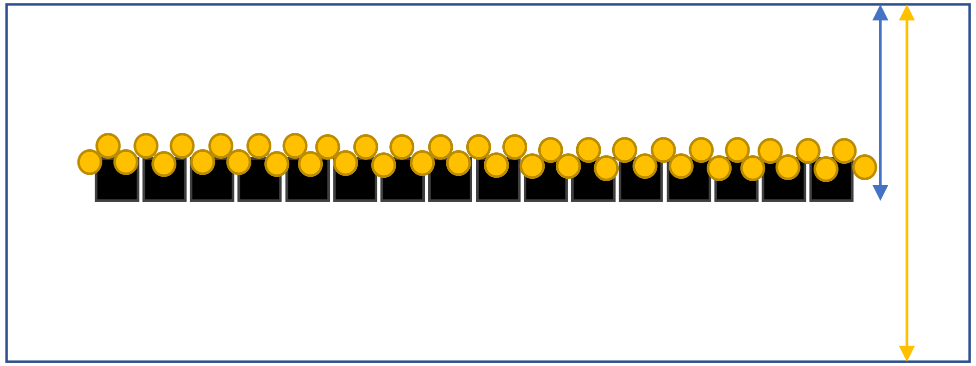
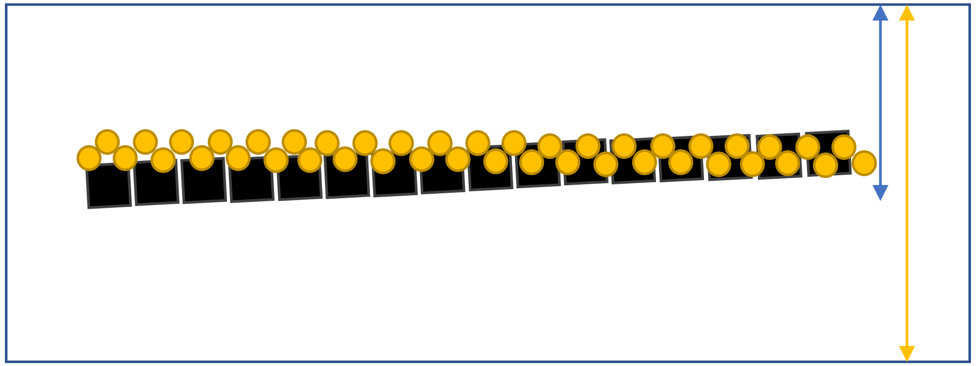


Photo sensors

Fibre



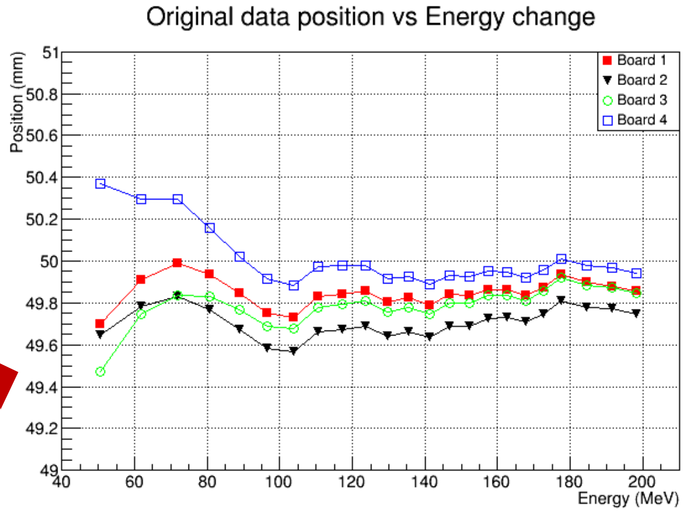


Calibration

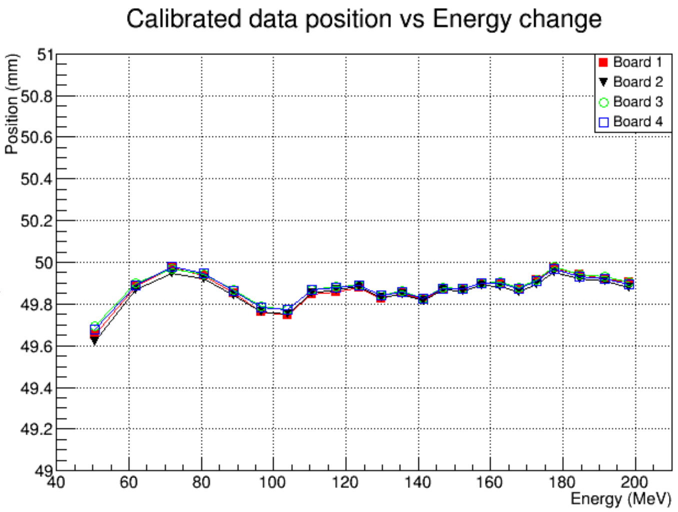
The calibration factor is calculated by using constant divided by the sum amplitude during the scan per each channel

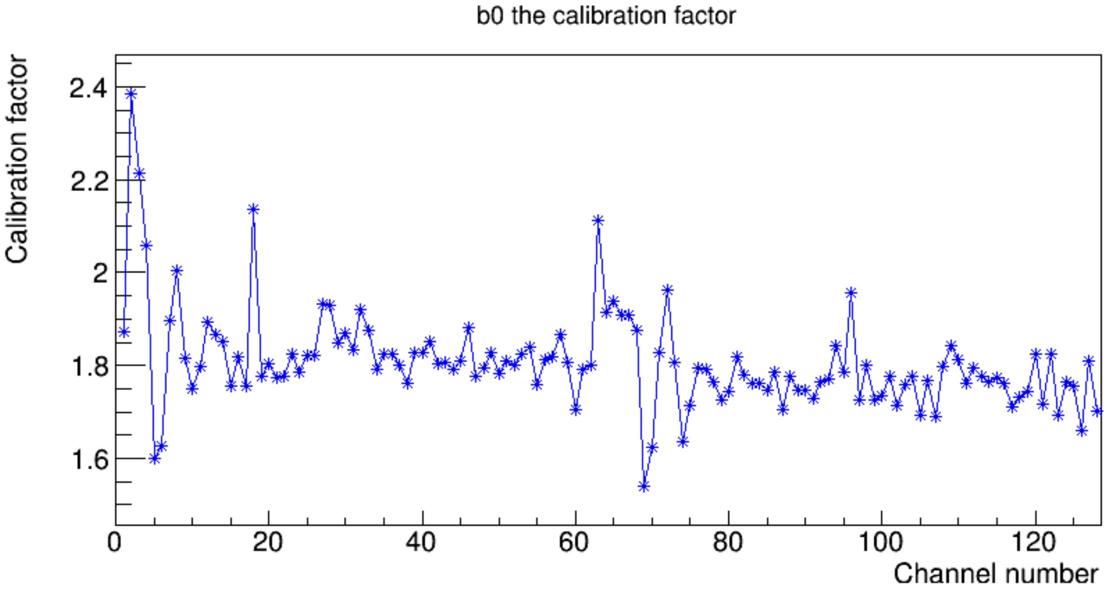
We have already proven that calibration can give much more reliable reconstruction information than non-calibrated one

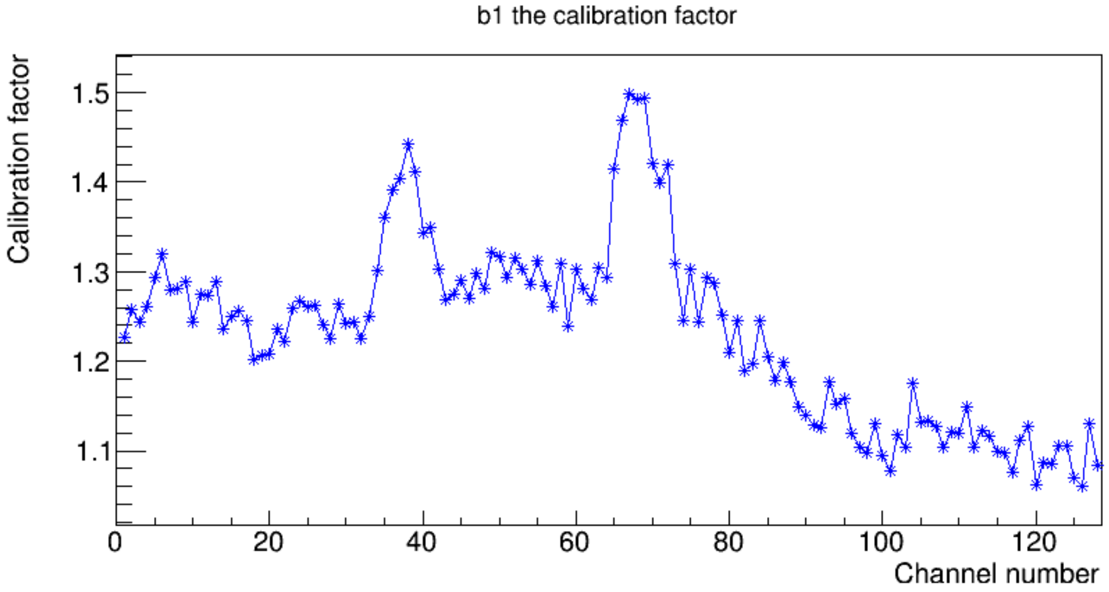
Uncalibrated



Calibrated + correct offset of the 4 boards







Calibration improvement possibility

Existing calibration have a very nice correction but still can we do it better?

- the sum signal of the scan of all the position of the fibre (all height)→ can not correct the light attenuation → Possible to correct at each scan row?
- constant divided by the sum signal as correction factor → Is there any other way to give better calibration factor?

Reconstruction algorithm

Low intensity – low SNR

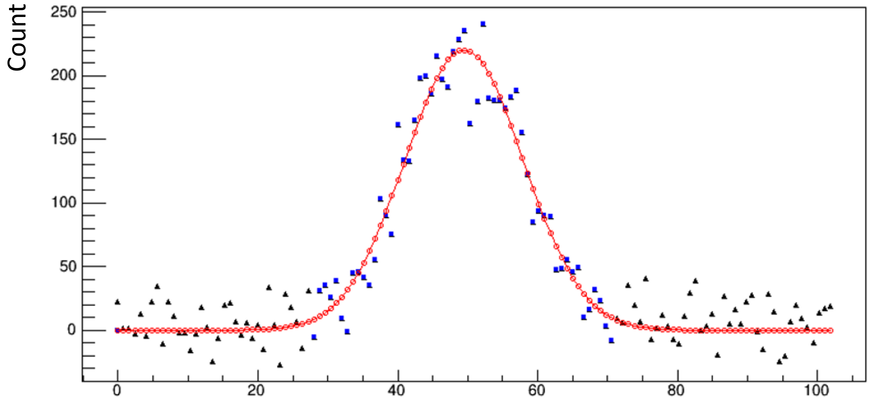
This algorithm should not only perform well in high SNR situation but also well for low SNR situations

Red: after reconstruction

Blue: the point which send to do reconstruction

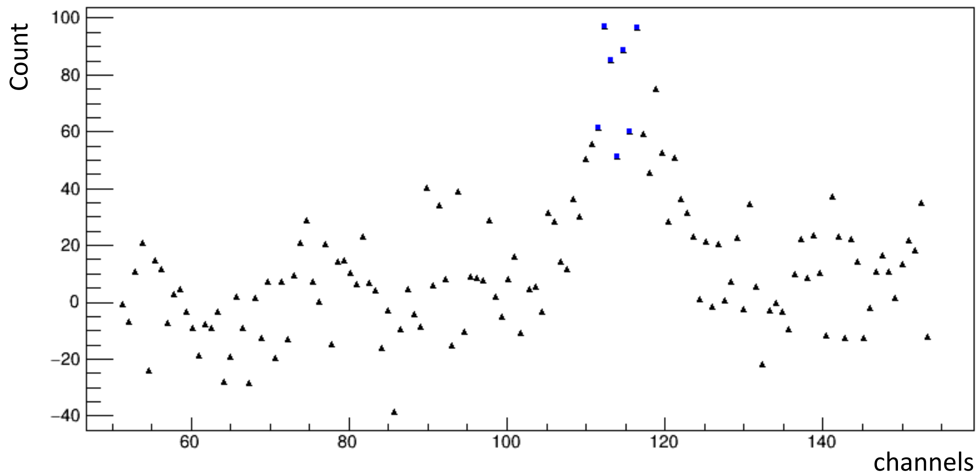
One frame

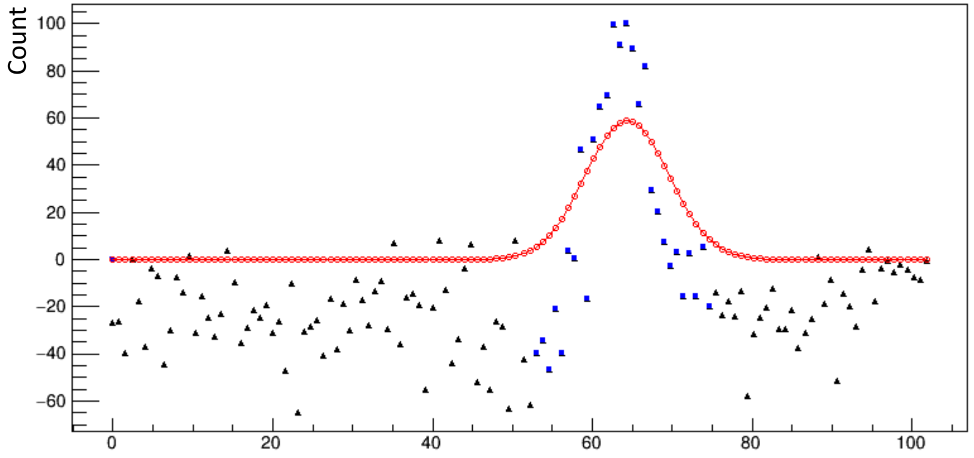
Proton: energy 221MeV intensity 205 10^6 s^{-1}



Example of bad reconstruction for low SNR

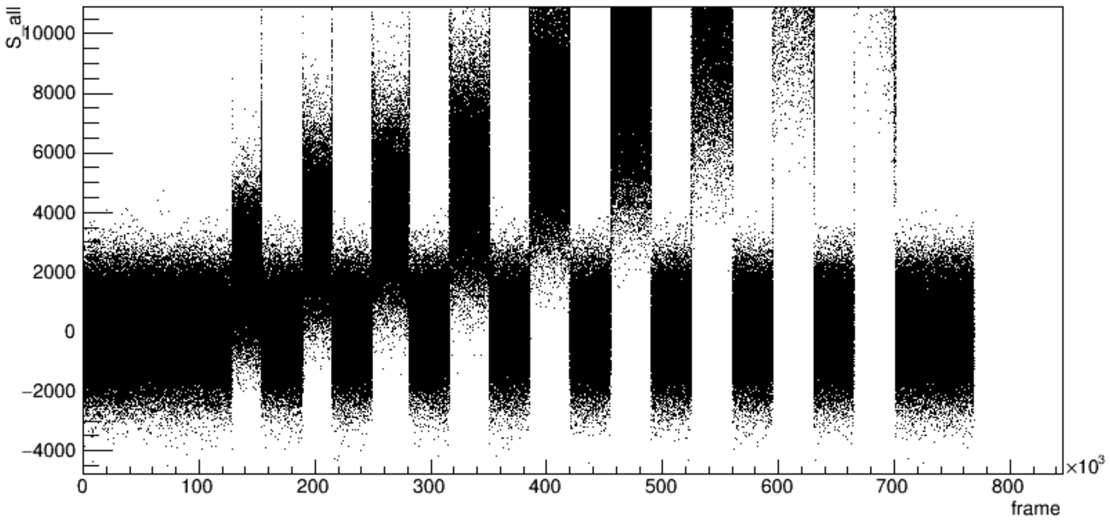
Proton: energy 221MeV intensity 126 10^6 s^{-1}





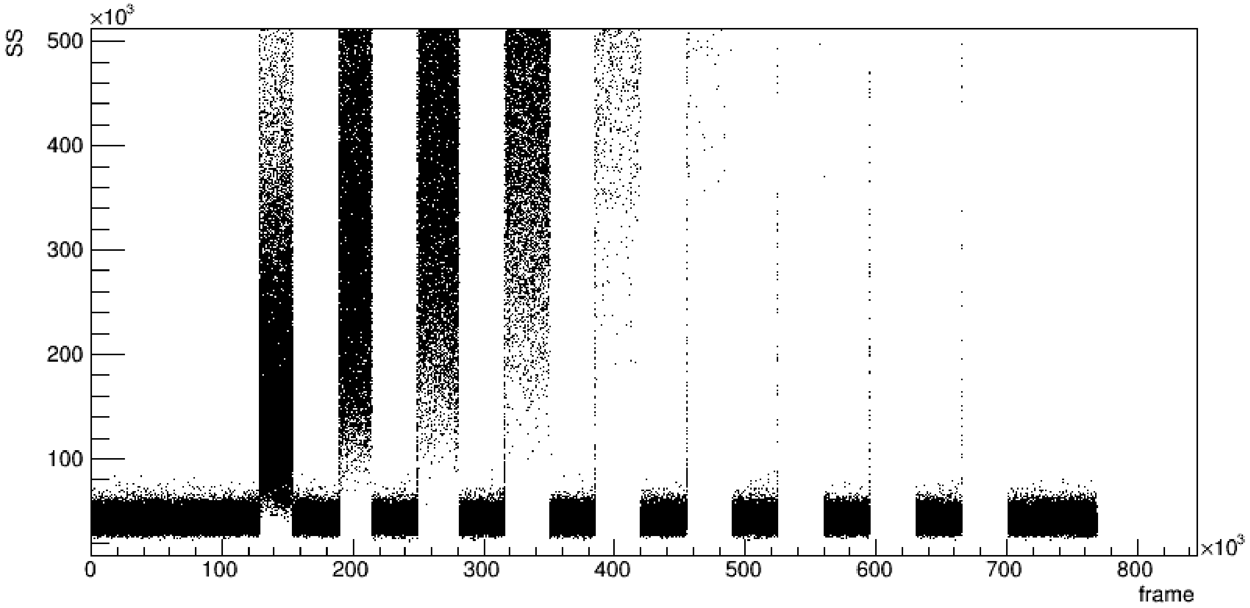
Beam-on state

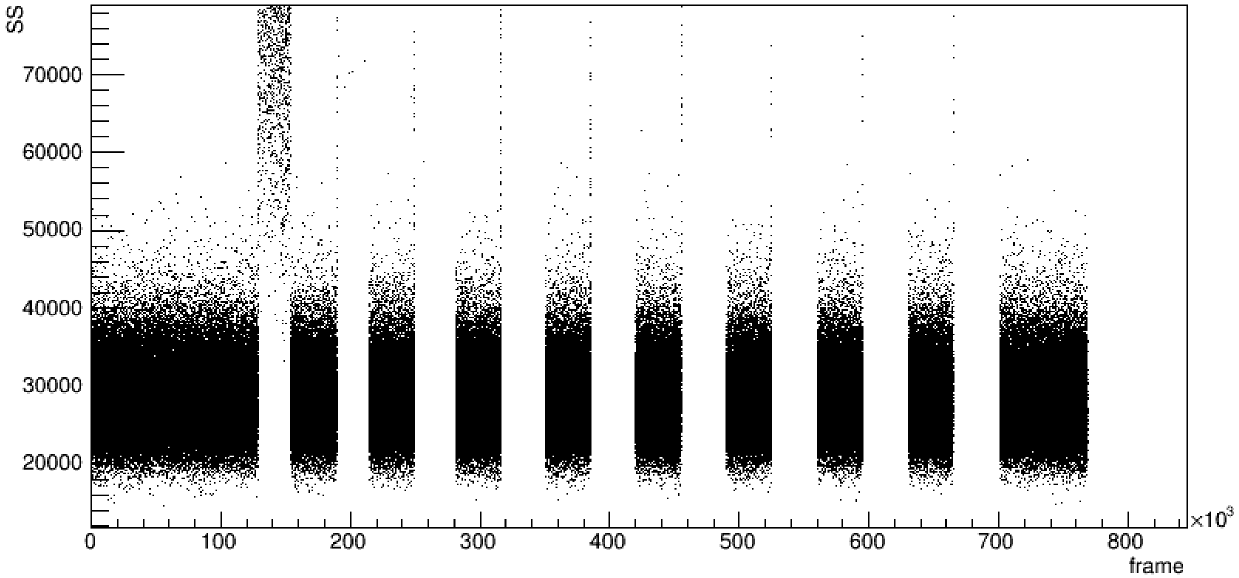
From the lowest intensity to highest intensity



- **Discriminate the "beam on" signal (when the beam comes this setting condition should be very sensitive to the signal changes)**

$$SS = N * \sigma^2 = \sum_{k=0}^{128} (A_k - A_{mean})^2 \qquad S_{all} = \sum_{k=0}^{128} A_k$$





Linear regression of gaussian distribution

<u>Example:</u>
Proton beam:
Energy = 221 MeV
Focus = 8.1 mm
Channel size: 8.1*6/2.355/0.8 = 26

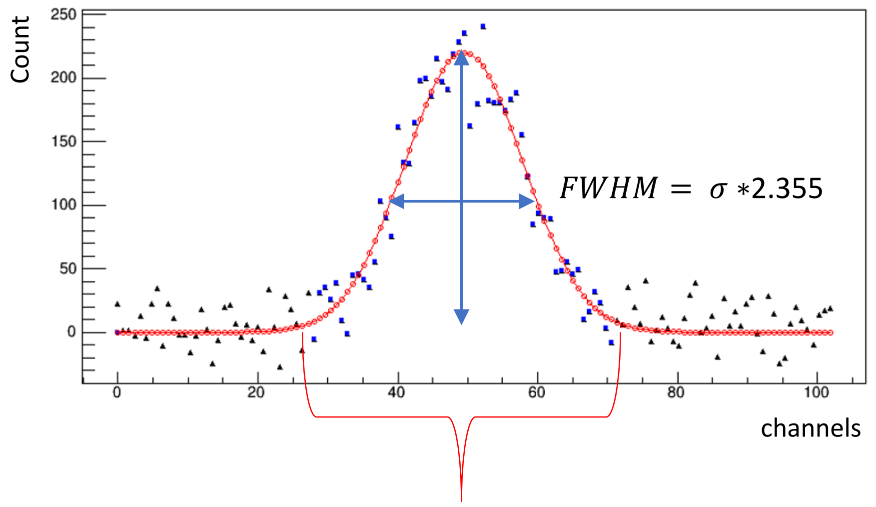
Quick and robust method to find out the position and width of the distribution

Linear regression → Highly depend on how we chose the data → to do the "**prediction**"

$$(x_1, f_1), (x_2, f_2), \ldots, (x_k, f_k), \ldots, (x_n, f_n)$$

- Set a basic threshold, select the longest cluster of data
- Take their average position (x_{mean})
- According to the x_{mean}, take the $\pm 3 * \boldsymbol{\sigma}$ length of the data

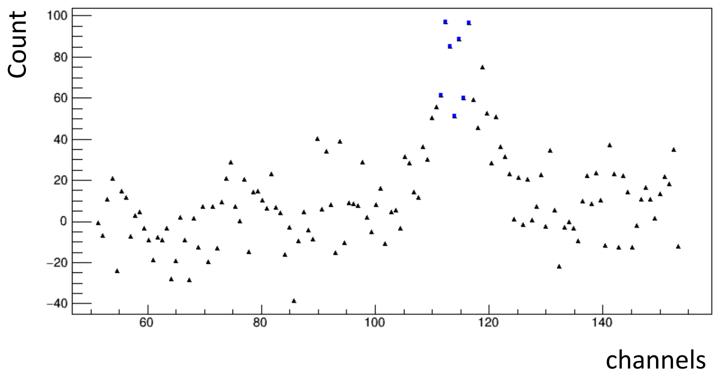
Proton: energy 221MeV intensity 205 10^6 s^{-1}

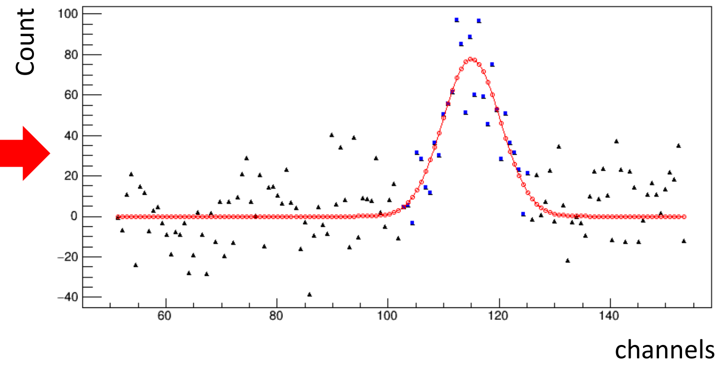


99.7% of the distribution: $6 * \sigma$

This is very meaningful for the low intensity → increase the sensitivity of the detector

Proton: energy 221MeV intensity 126 10^6 s^{-1}





Chose proper data set

Subtract the noise level

Subtract the noise base level→ there exist the fluctuation of the noise level

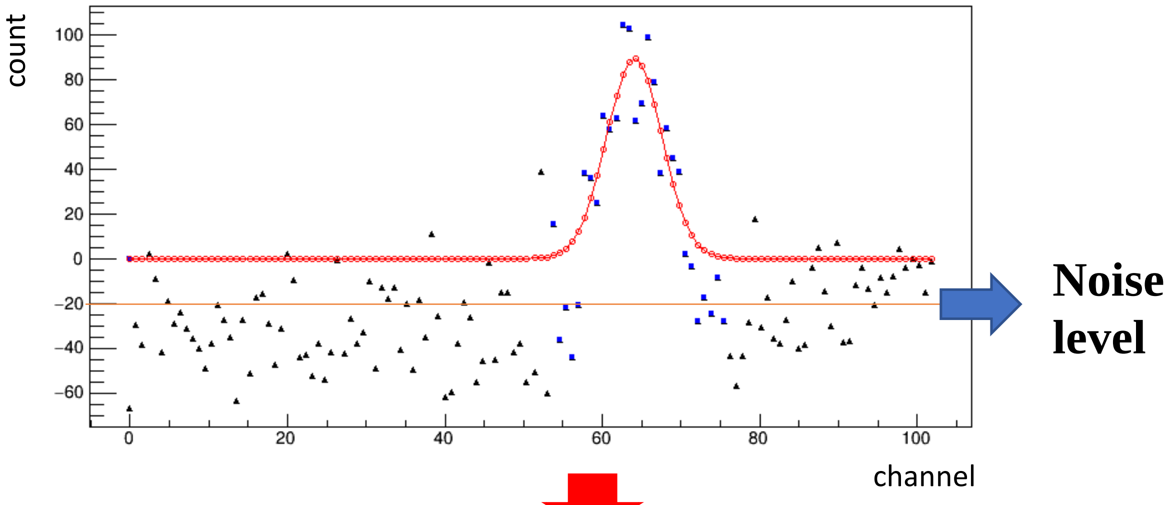
Blue point :
the data which are sending to do the reconstruction

Red point: reconstruction result

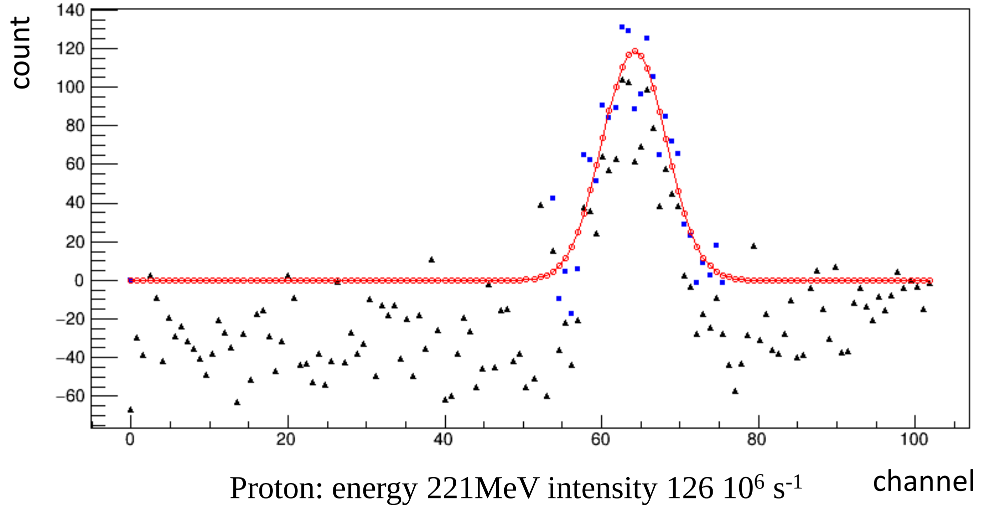
Black point: original data

Sending the $(x_1, f_1), (x_2, f_2), \ldots, (x_k, f_k), \ldots, (x_n, f_n)$ to do the linear regression (based on integration-Jean Jacquelin)

Original



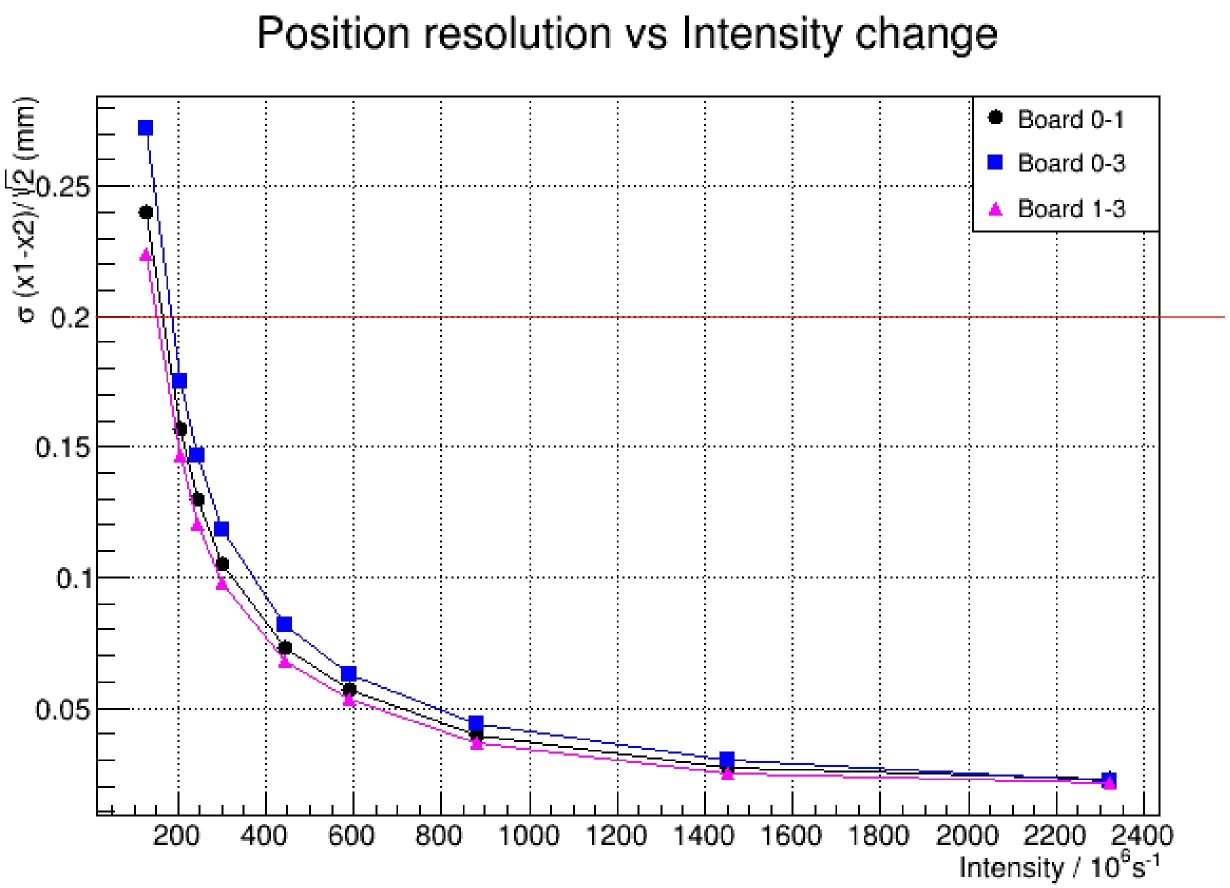
Subtract the noise level



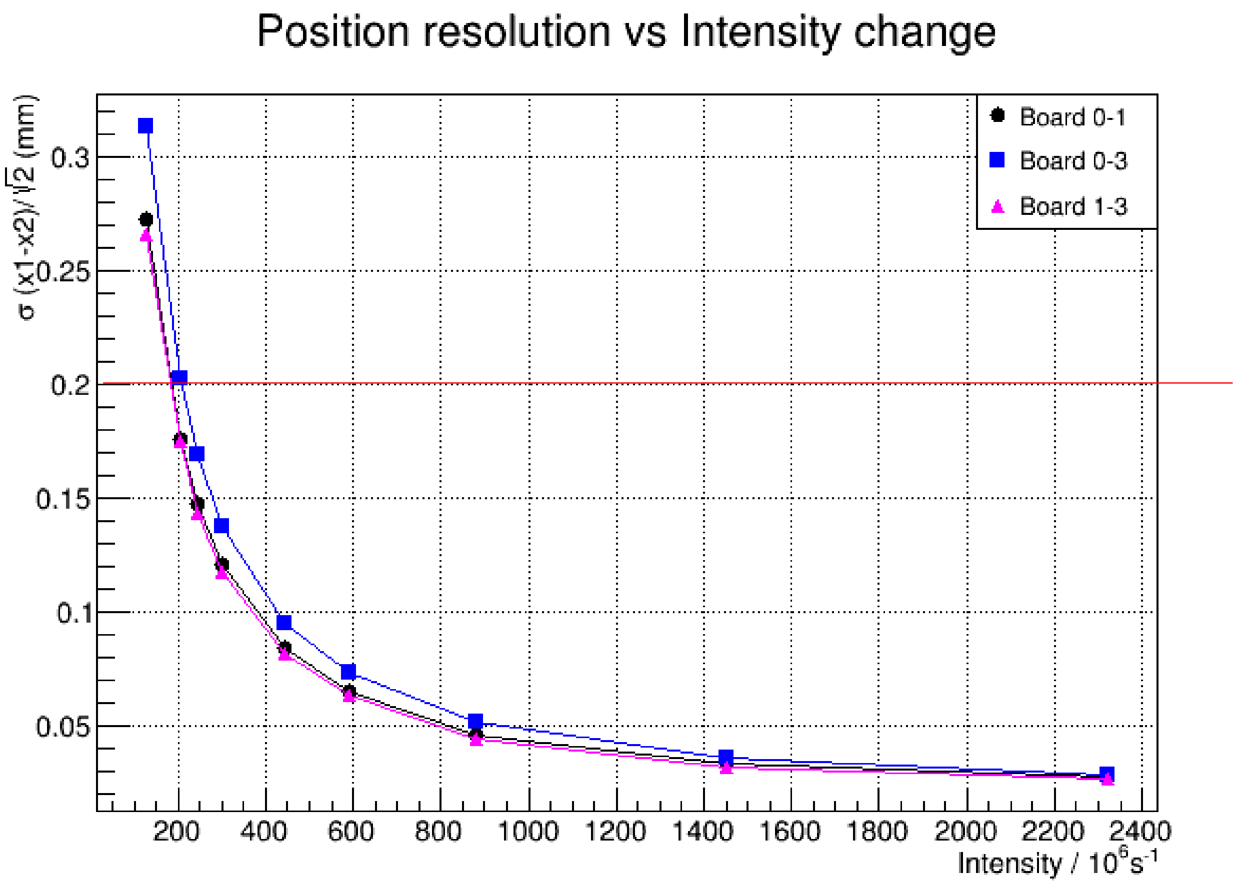
Proton: energy 221MeV intensity 126 10^6 s^{-1}

Proton with energy 221 MeV / intensity scan

Gaussian fitting



Gaussian Linear regression



$\mathbf{100\mu s}$ per each frame for this detector

For low intensity, we can change the integration time to get better resolution

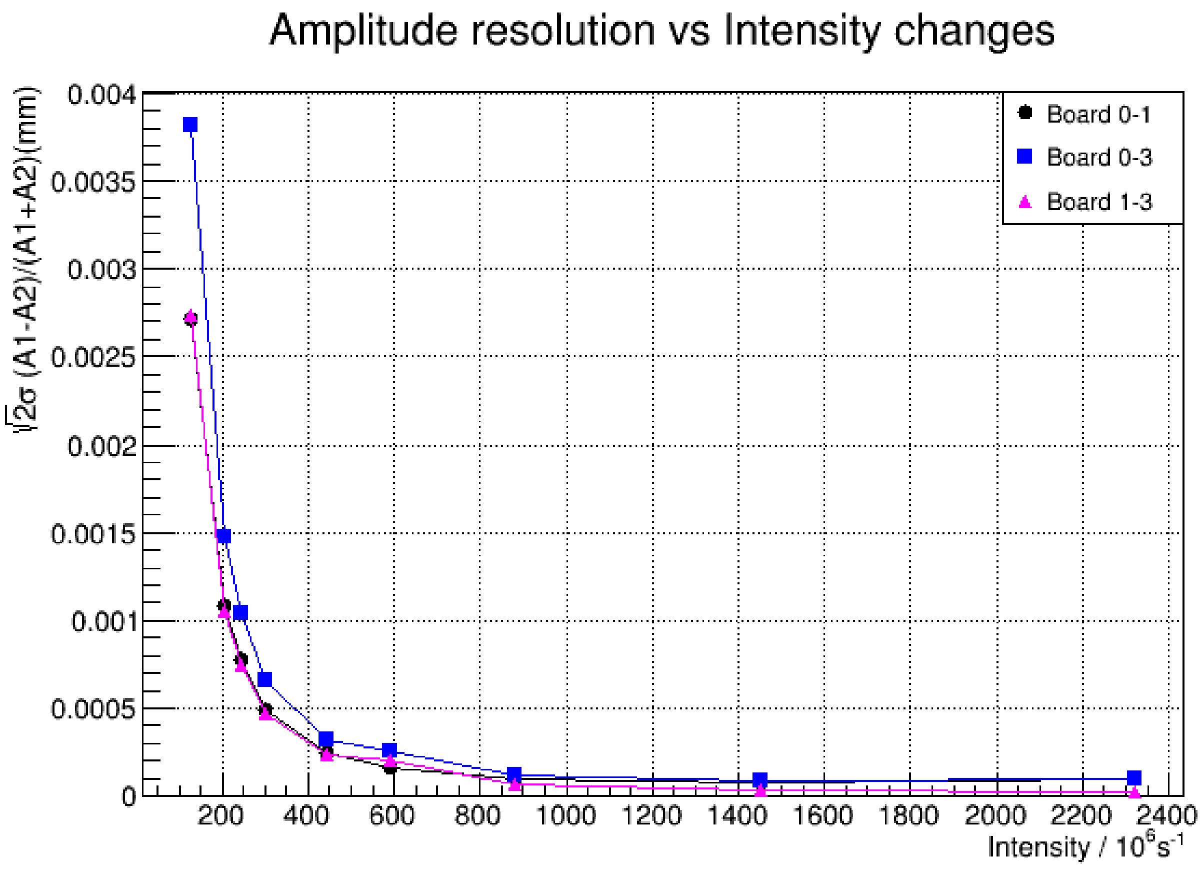
Proton with energy 221 MeV / intensity scan

Gaussian fitting

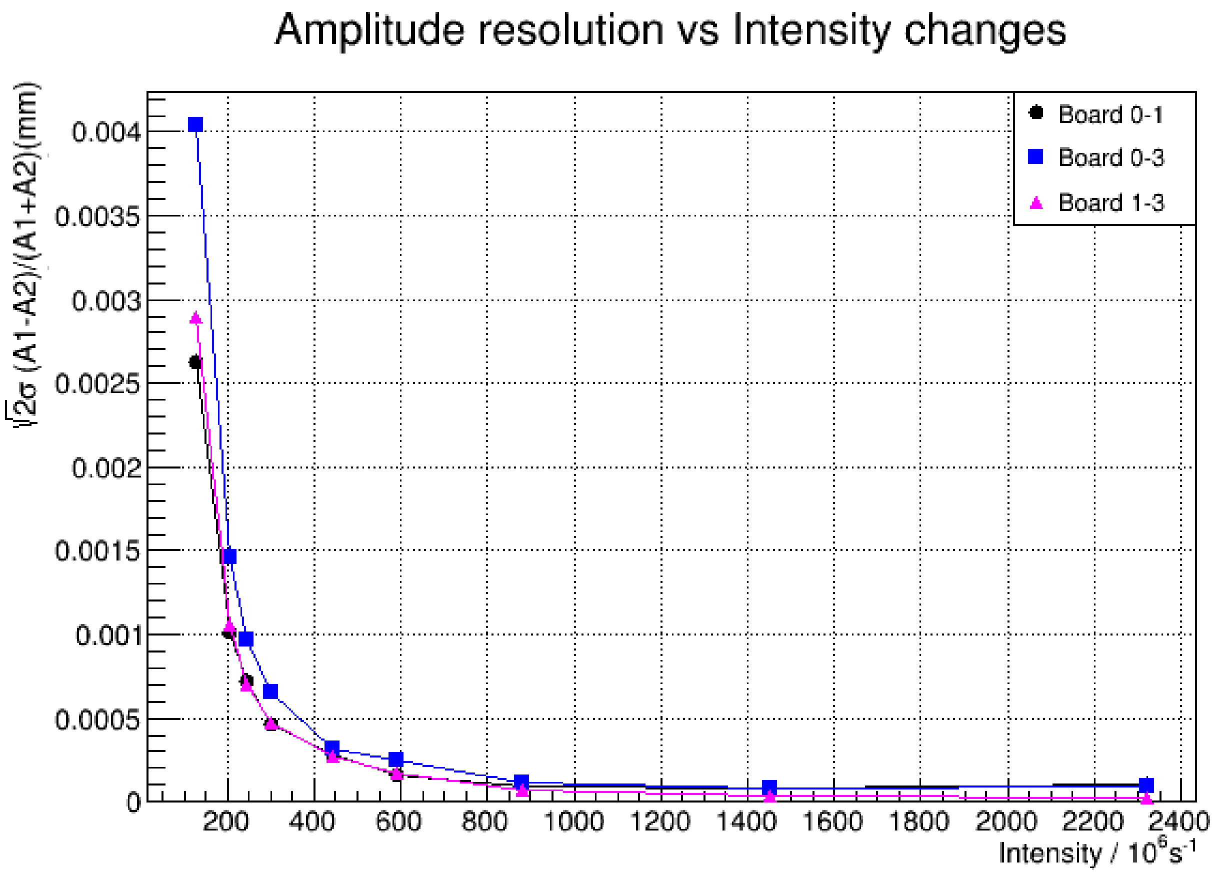
Gaussian Linear regression

Proton with energy 221 MeV / intensity scan

Gaussian fitting



Gaussian Linear regression

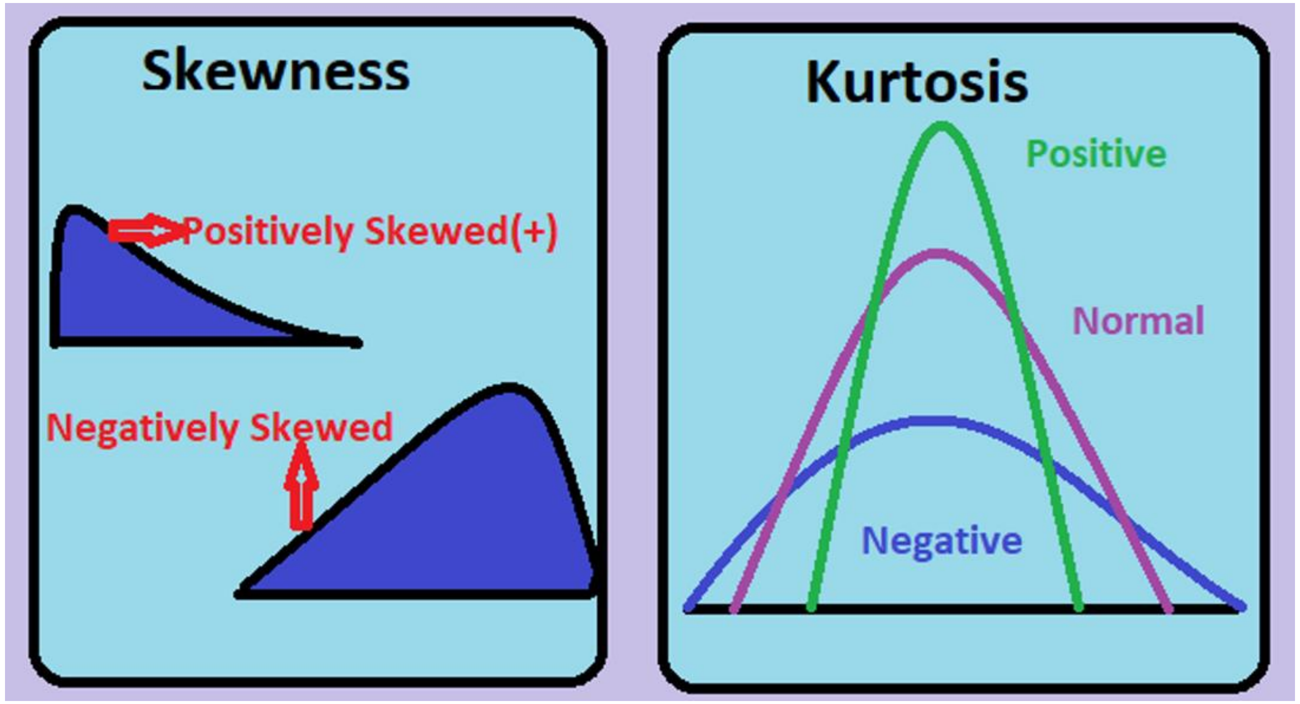


Shape of the beam and reconstruction difference

- What are **Gaussian fitting** and **linear regression** differences based on the same data?
- Is the beam gaussian distribution?

The **kurtosis** measures how sharply peaked a distribution is, relative to its width. The kurtosis is normalized to zero for a Gaussian distribution.

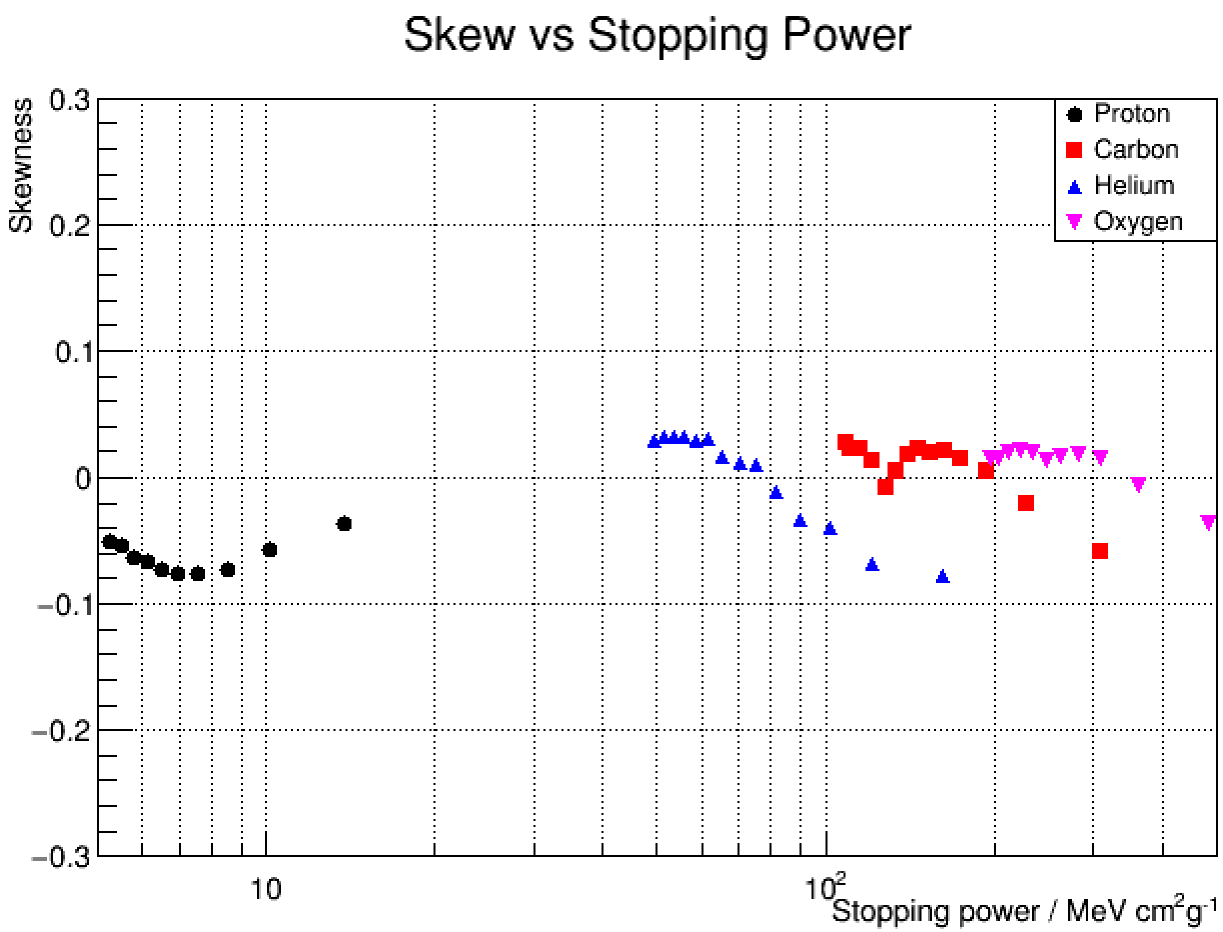
The **skewness** measures the asymmetry of the tails of a distribution.



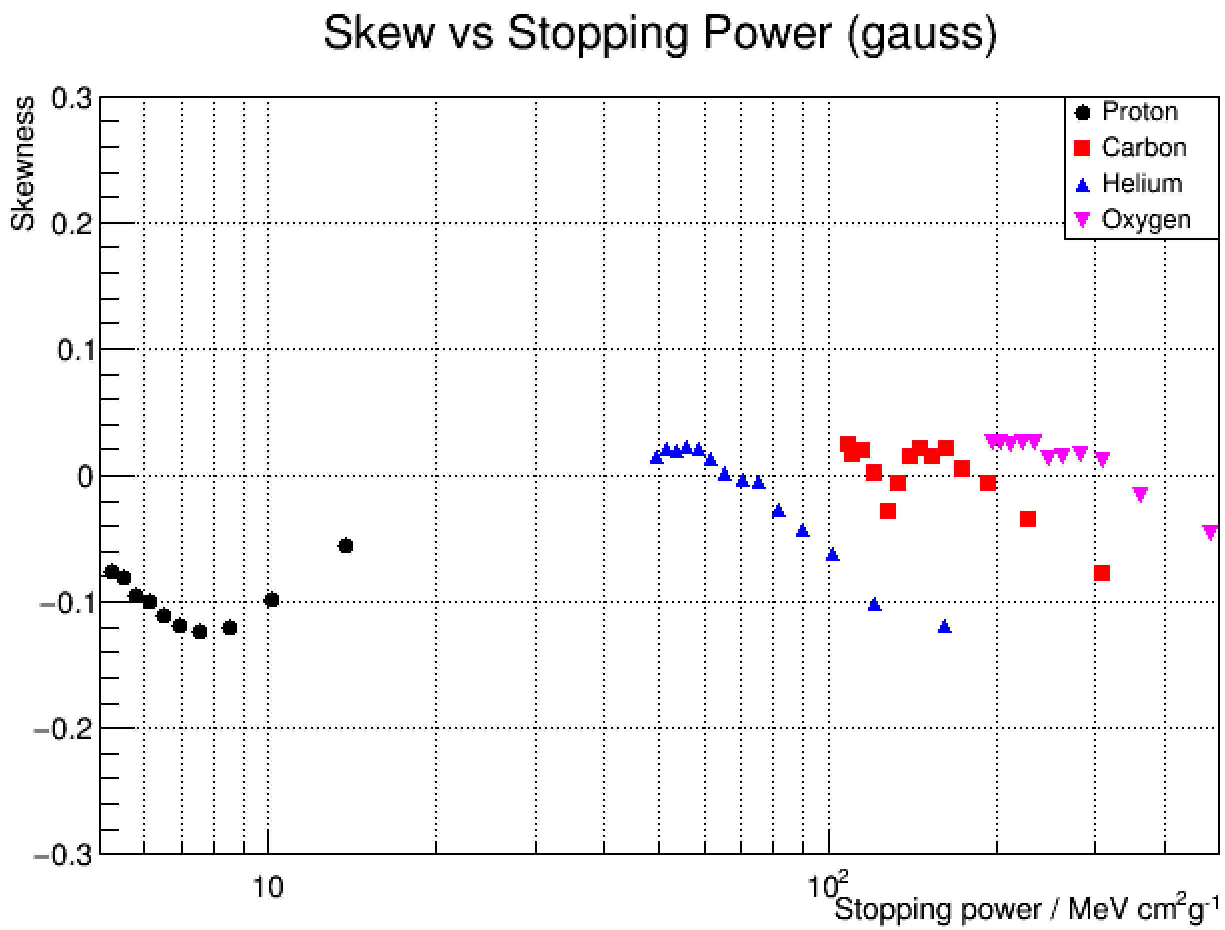
$$skew = \frac{1}{N}\sum\left(\frac{x_i-\hat{\mu}}{\hat{\sigma}}\right)^3$$

$$kurtosis = \left(\frac{1}{N}\sum\left(\frac{x_i-\hat{\mu}}{\hat{\sigma}}\right)^4\right) - 3$$

Linear regression



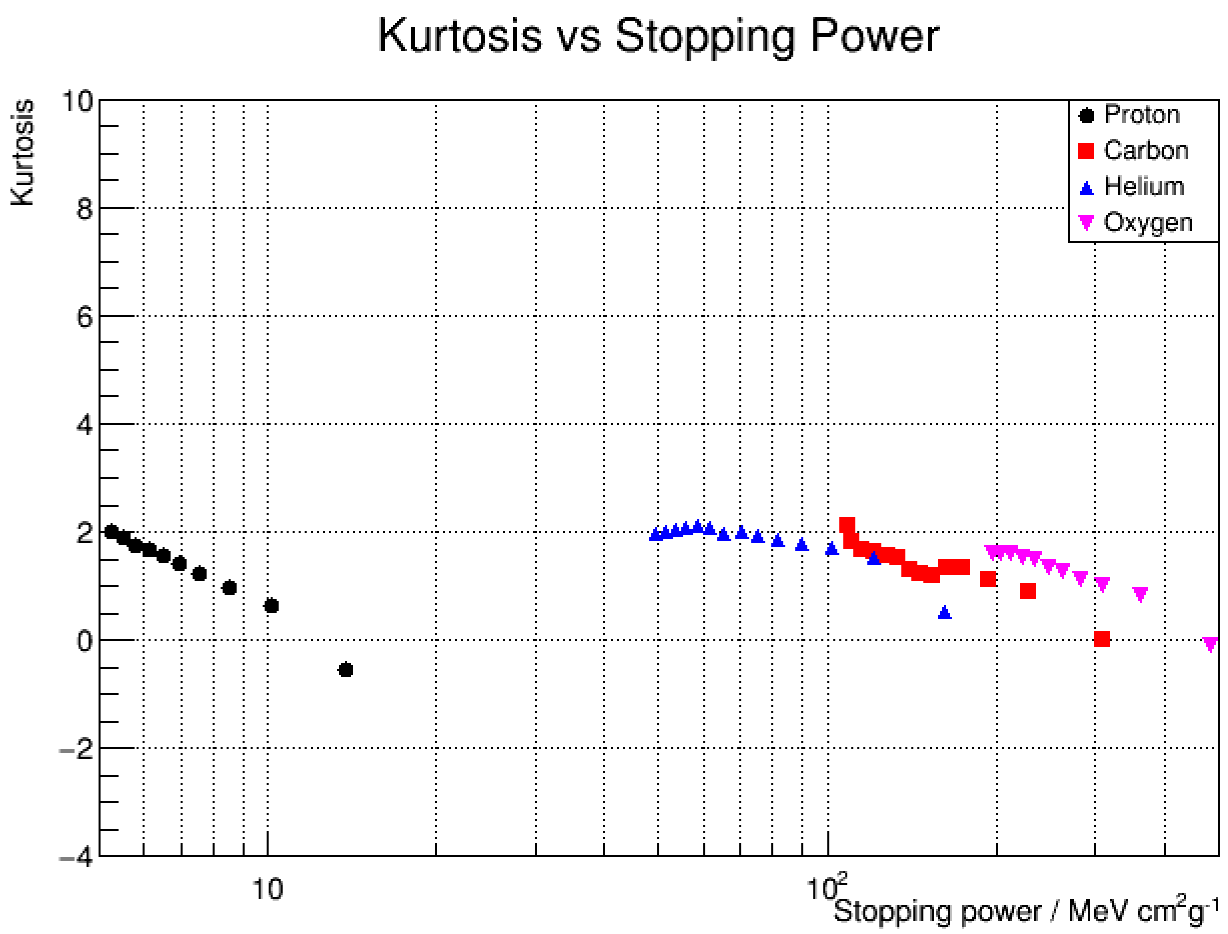
Gaussian fitting



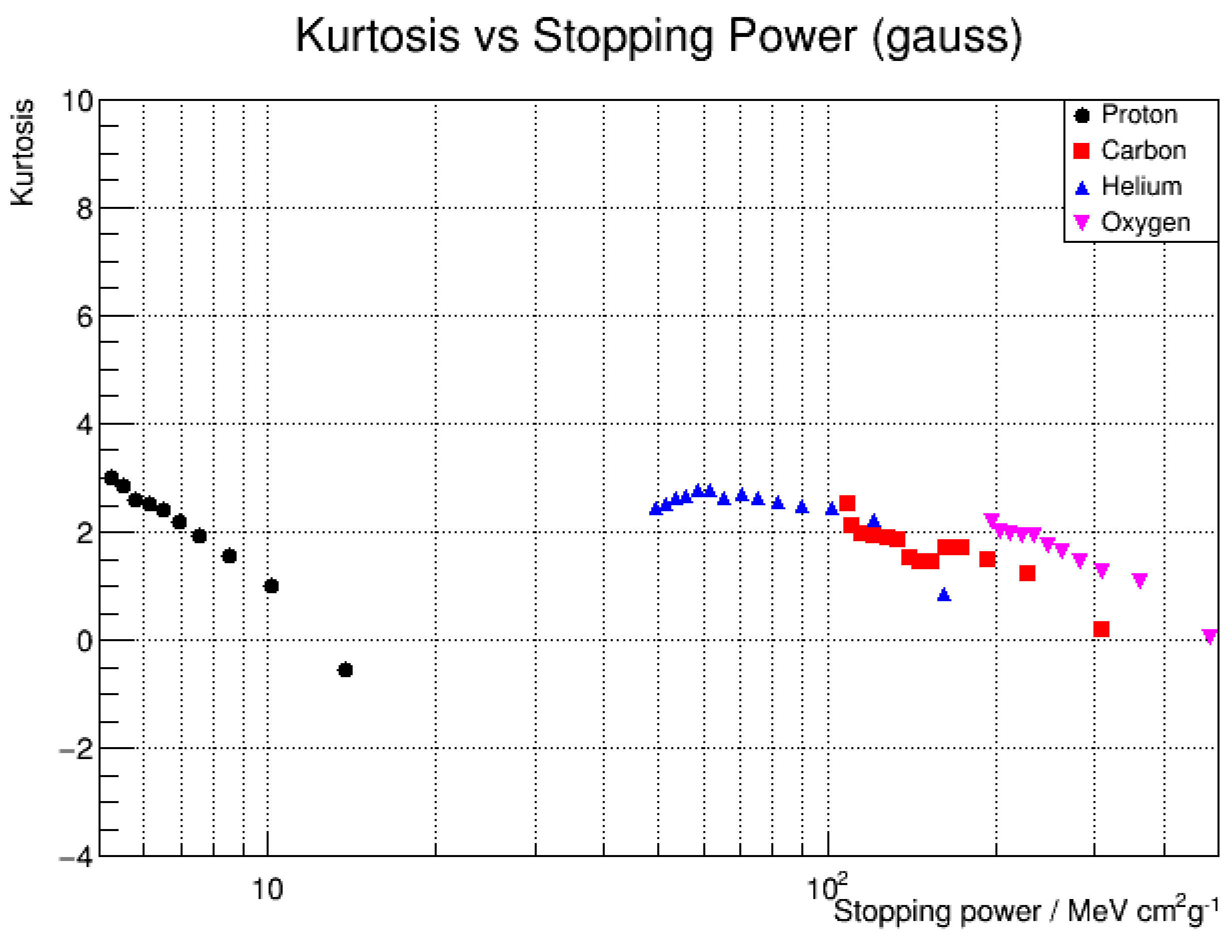
The skew is related to:

- **Different Ion types' shape are different (from HIT)**
- **Reconstruction**

Linear regression



Gaussian fitting

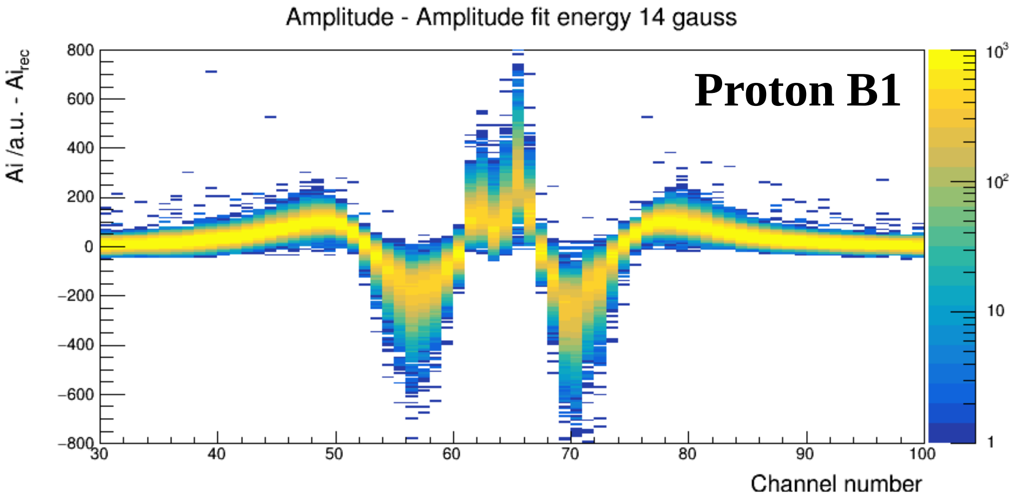


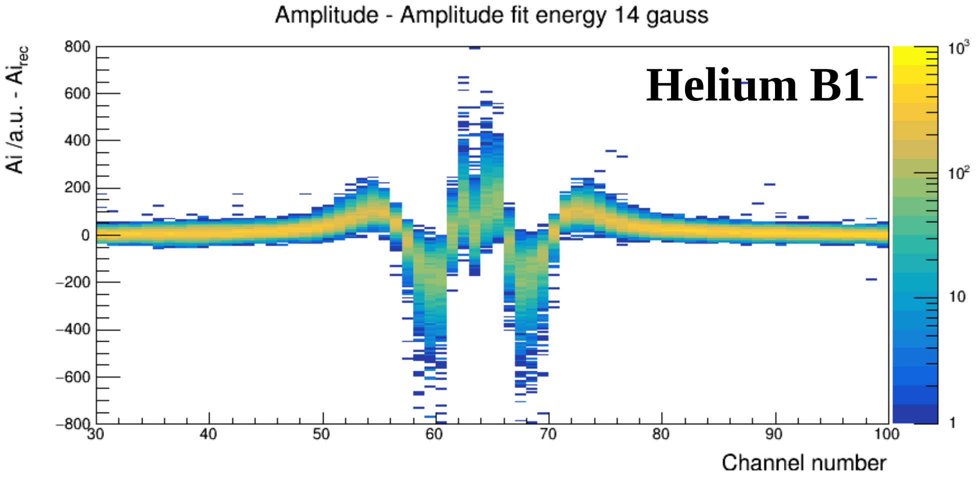
The kurtosis is largely related to:
Reconstruction

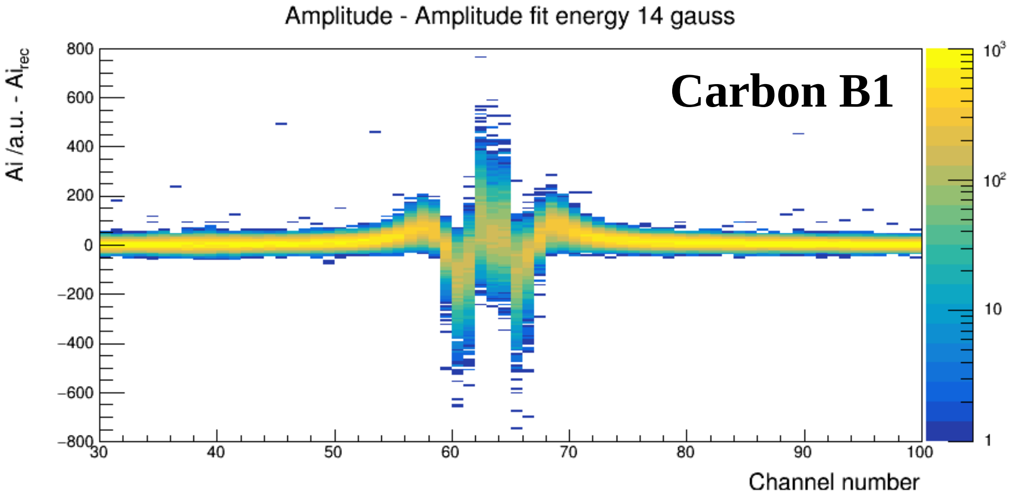
The subtraction between the real signal and reconstruction

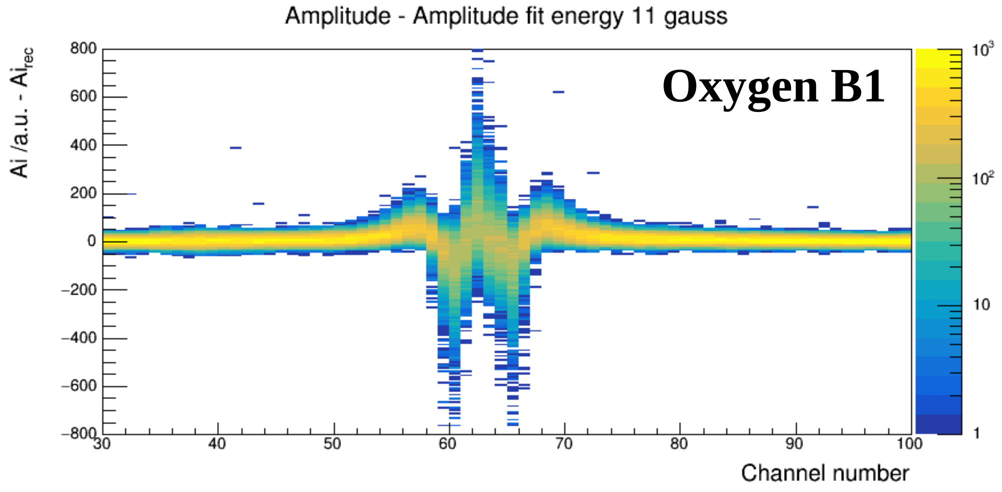
(Intensity 2322 10^6 s^{-1})

Beams are not perfect gaussian distribution!









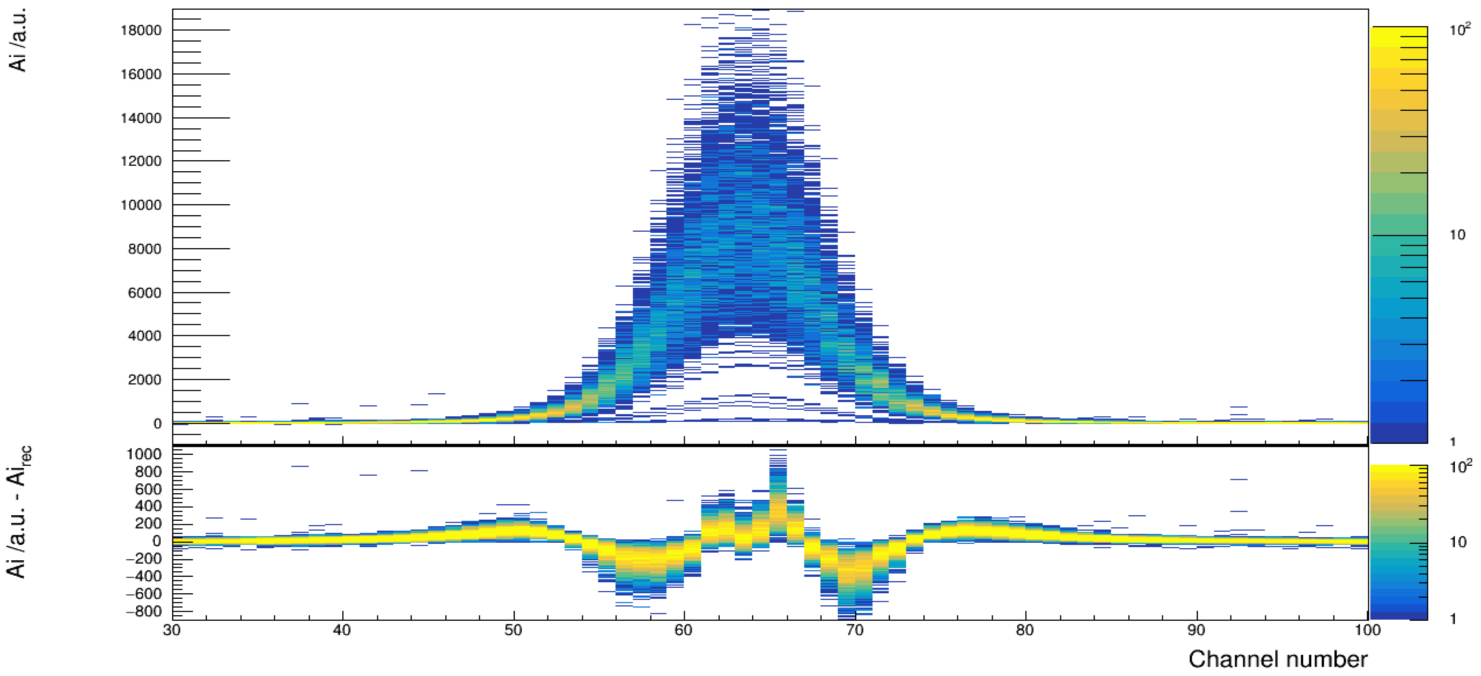
The ratio

Helium energy: 162 MeV Intensity 2322 10^6 s^{-1}

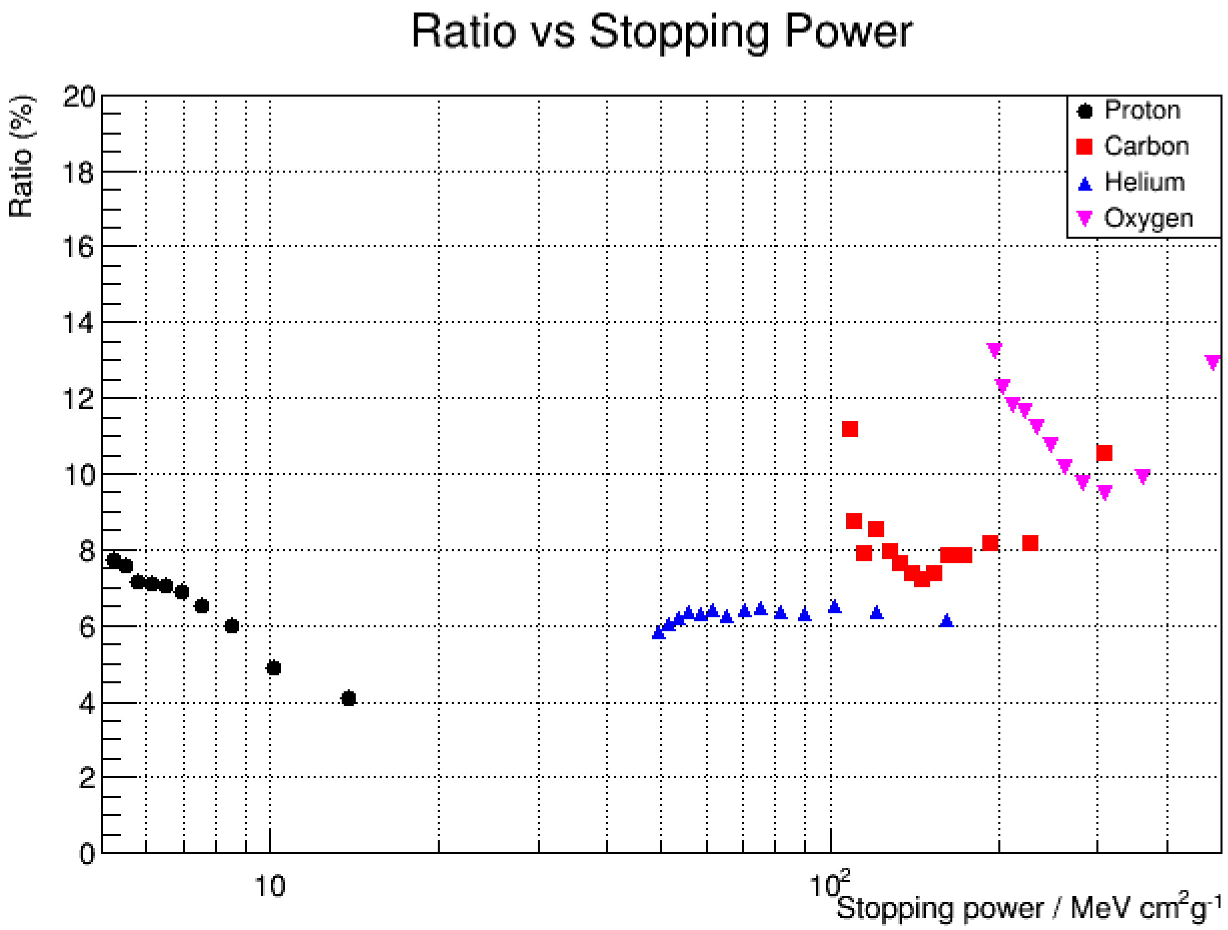
<u>The ratio:</u>

Shows how much is the proportion of difference between the reconstruction signal and real signal to the real signal

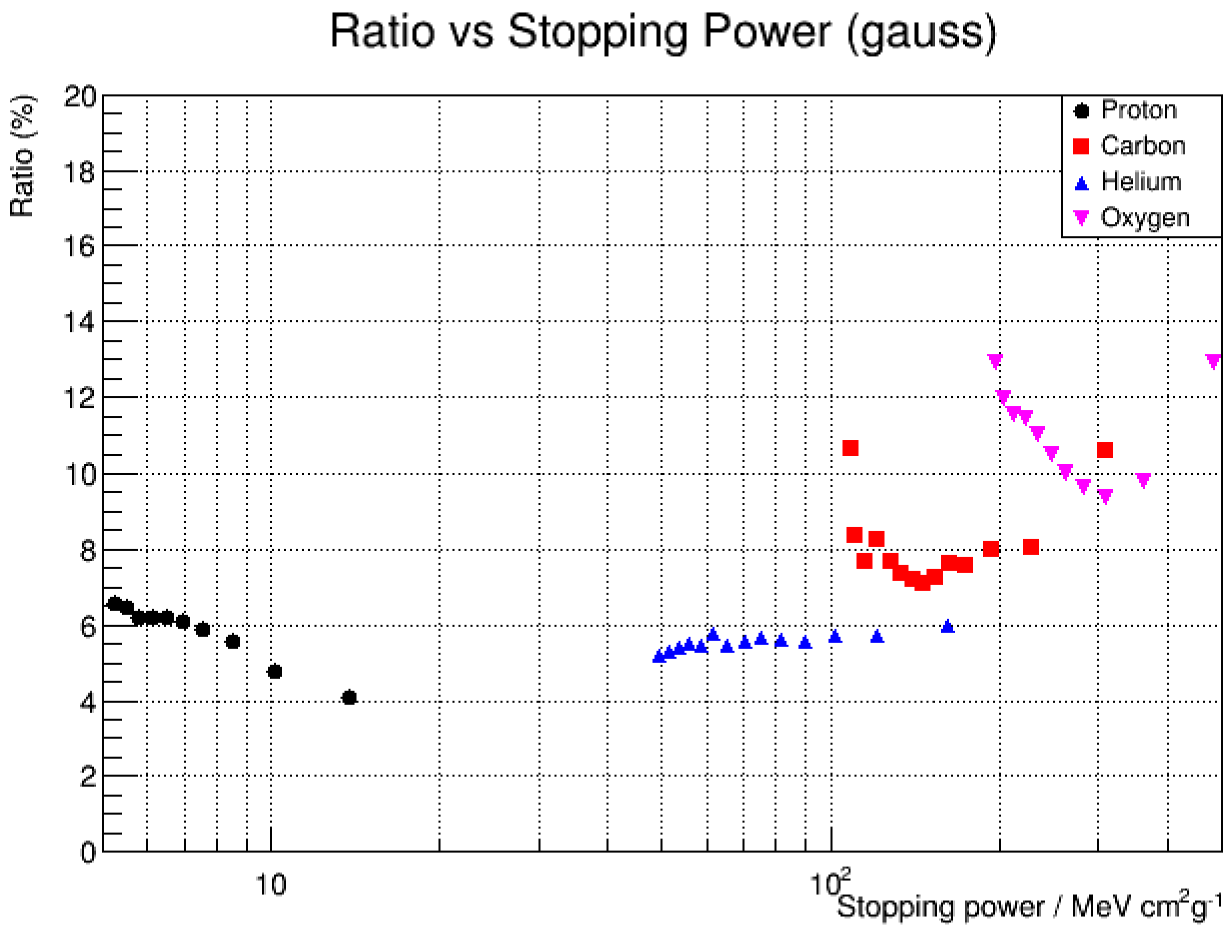
the average of each frame's
Sum(abs(Ai_{rec} – Ai)) / Sum(abs(Ai))



Linear regression



Gaussian fitting



Linear regression have slightly bigger ratio than the gaussian fitting

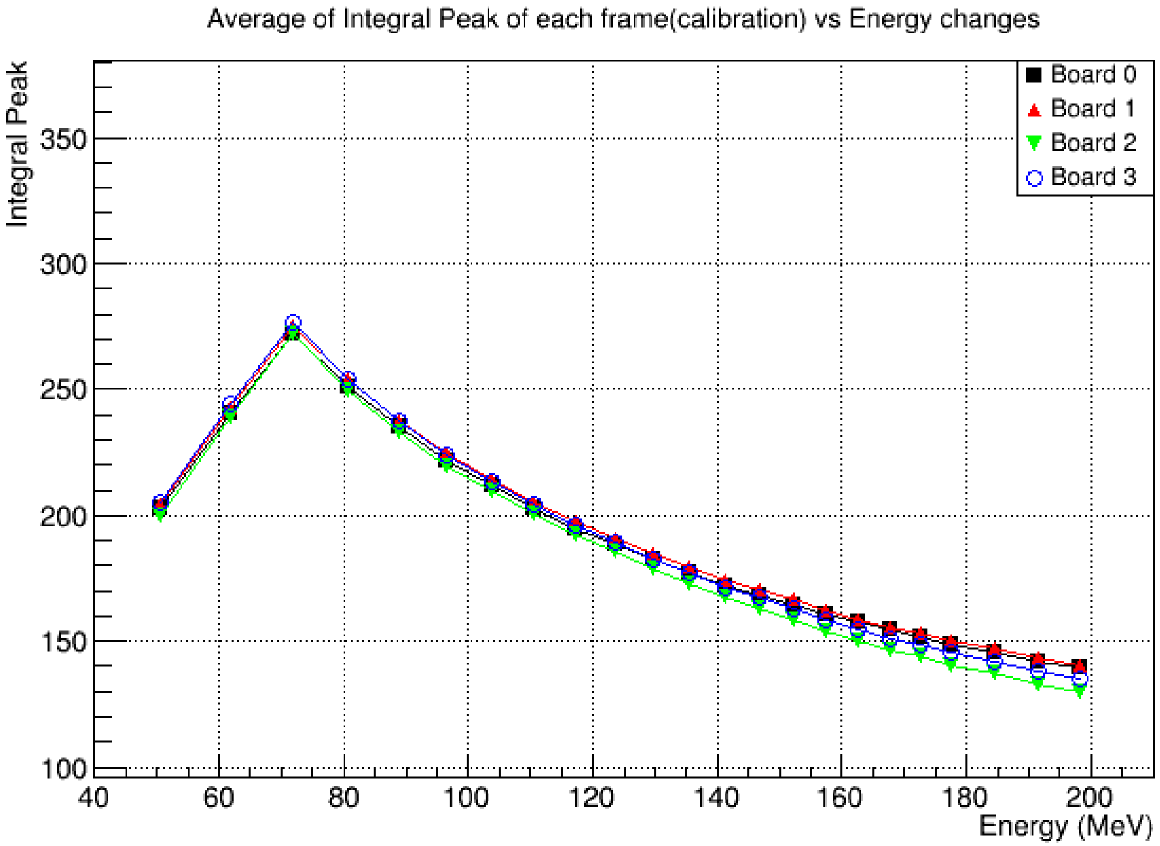
For Carbon and oxygen the shape of the beam is narrow !!! When the Stopping power is high→ Low energy→ the intensity is lower than setting value!!!

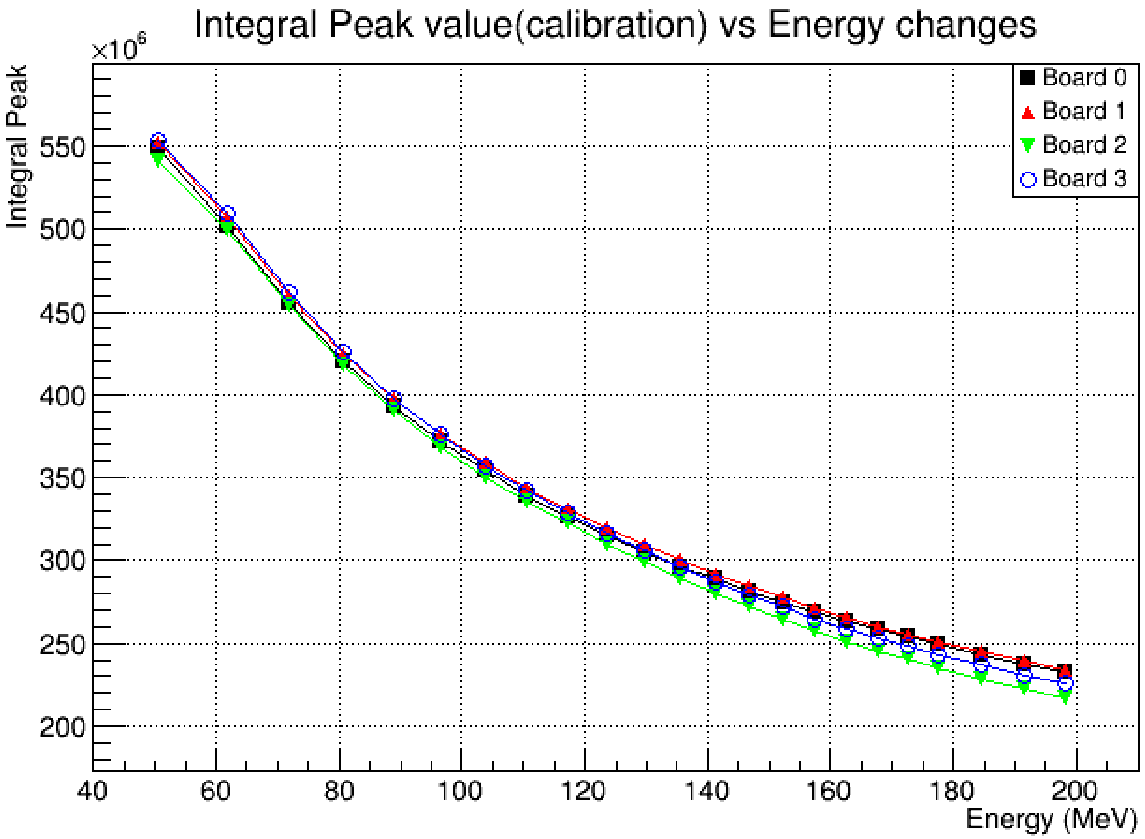
HIT setting feature

Below 70 MeV the intensity is lower than the setting
So the integration of the peak of each frame is smaller than expectation

Even though the intensity is lower than setting, but the particle numbers are the same

particles="250 000 000"



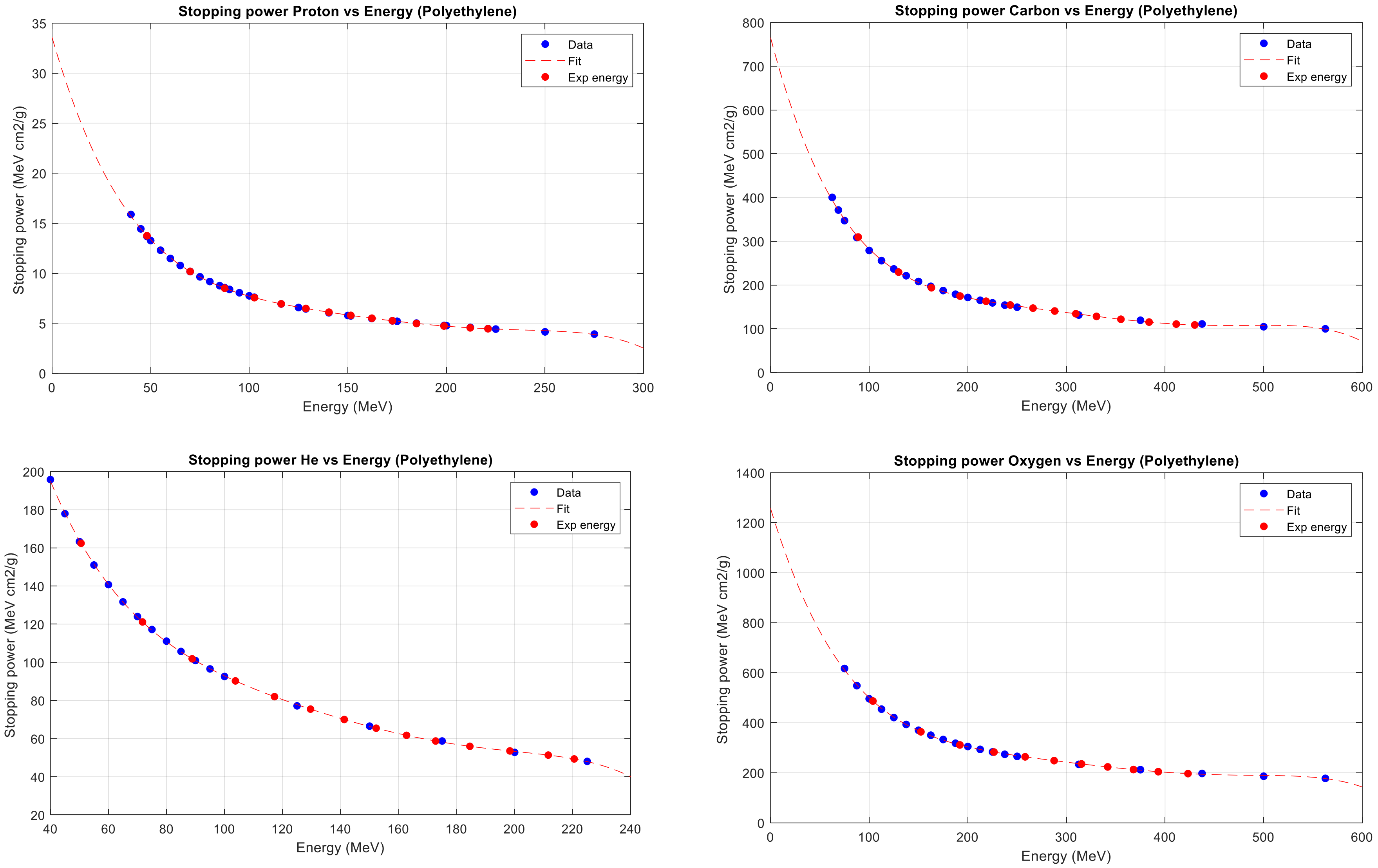


Stopping power decreases with higher energy

Energy - stopping power

Transform the energy towards the corresponding material stopping power

Protons and alphas: PSTAR and ASTAR.
Carbon and oxygen: MSTAR

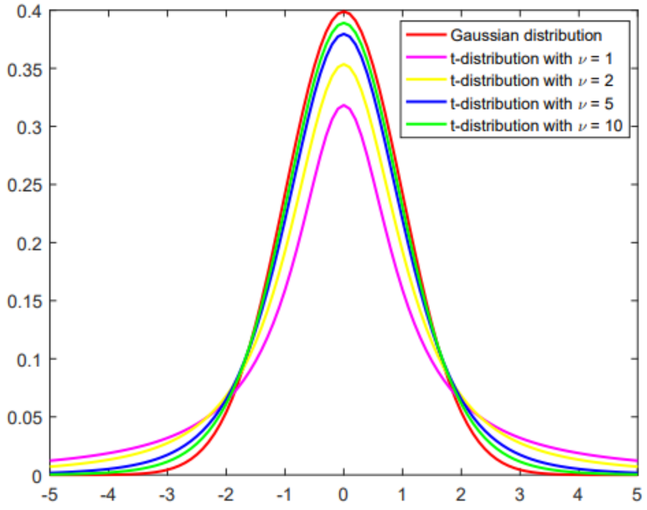


Future work

Gaussian distribution

Student T distribution

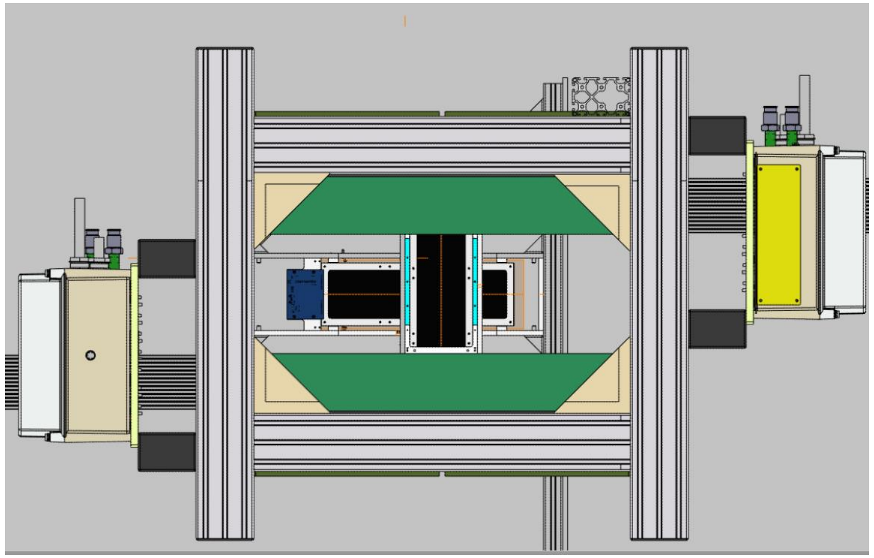
$$f(x) = \frac{\Gamma((\nu+1)/2)}{\sqrt{\nu\pi}\,\Gamma(\nu/2)(1+x^2/\nu)^{(\nu+1)/2}}$$



Double gaussian

Test in magnetic field

Test without the beam in Helmholtz coil



Investigate research of the MR-guidance ion beam therapy→ The targeting accuracy of proton therapy (PT) for moving soft-tissue tumors is expected to greatly improve by real-time magnetic resonance imaging (MRI) guidance.

↓

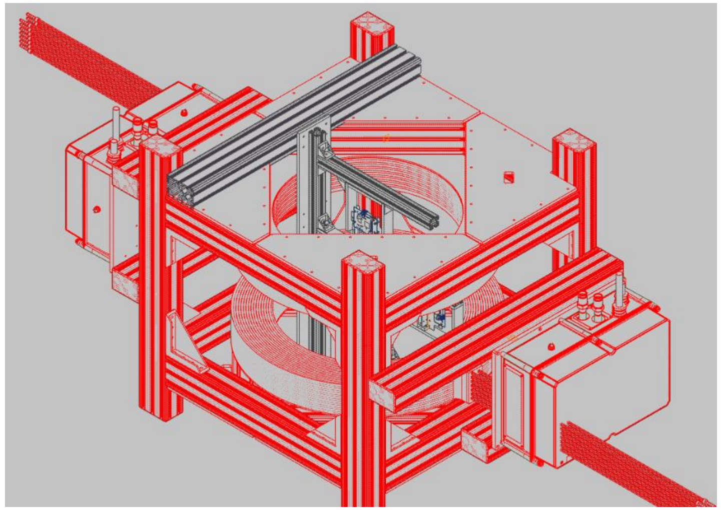
how magnetic field effect beam-on monitor detector ?

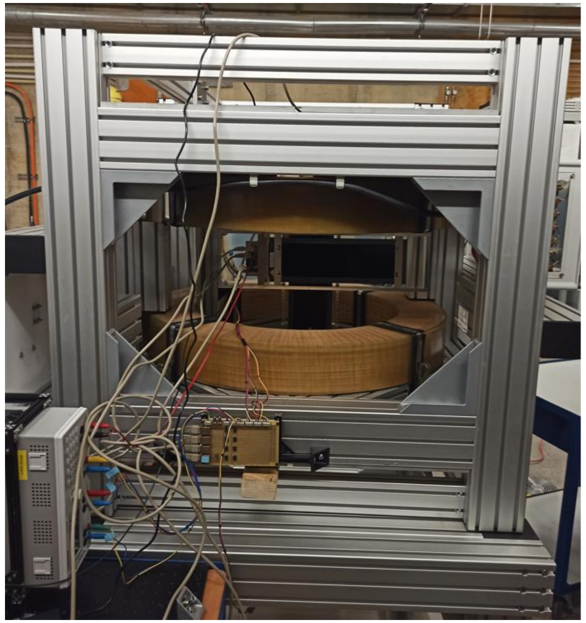
→ no impact on scintillating fibre (made from plastic, no electron signal)

→ only electronic is affected

↓

Put one vertical and one horizontal detector inside the Helmholtz coil





Operation in magnetic field

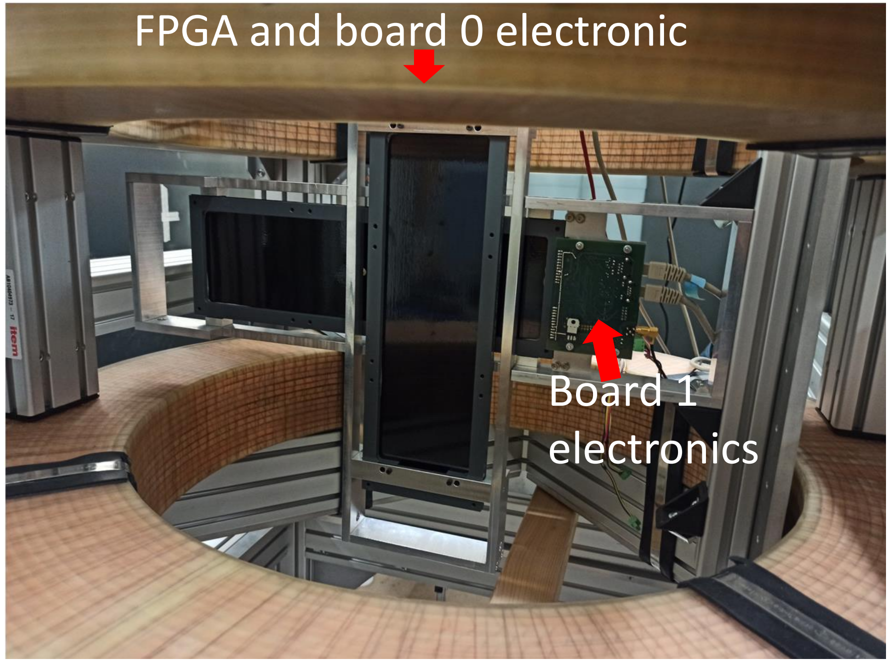
Gradually increase the magnetic field

Board 1 display frozen for several times (begin at **50 mT** maximum flux density of the Helmholtz coil)

Magnetic field affect electronics

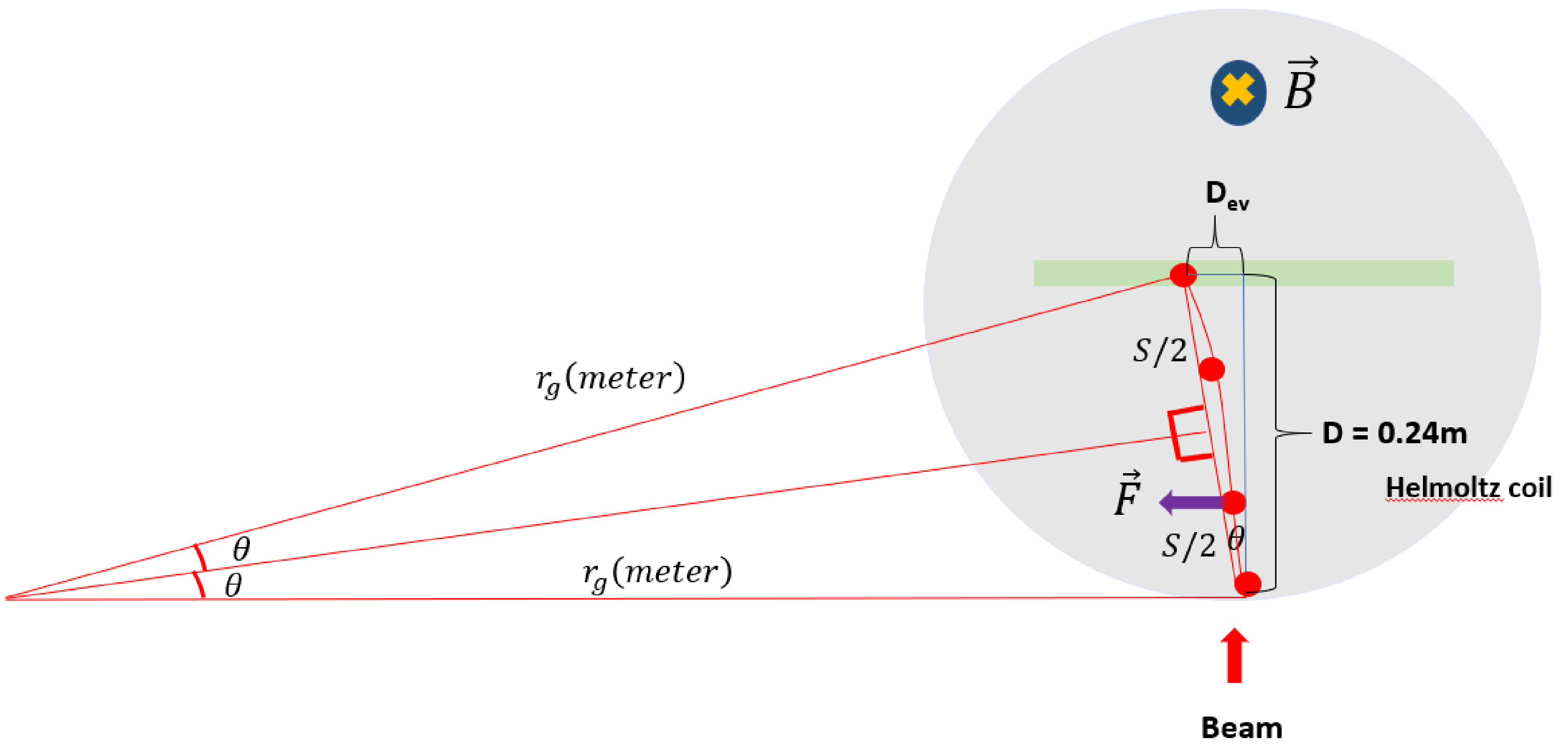
- New detector system under development with electronics outside magnetic field.
- Use optical fibre to extract signal without loss of spatial resolution.
- For now: Only measurements at low magnetic fields

Mg set (mT)	Electronics (center) (mT)	FPGA point (mT)
~10	~10.37	~5
~20	~20.6	~15
~100	~104	~75



Inferences

Intersecting surface of the Helmholtz coil



Magnetic field increase:

D_{ev} increase

$$D_{ev} \propto \vec{B}$$

Momentum increase:

D_{ev} decrease

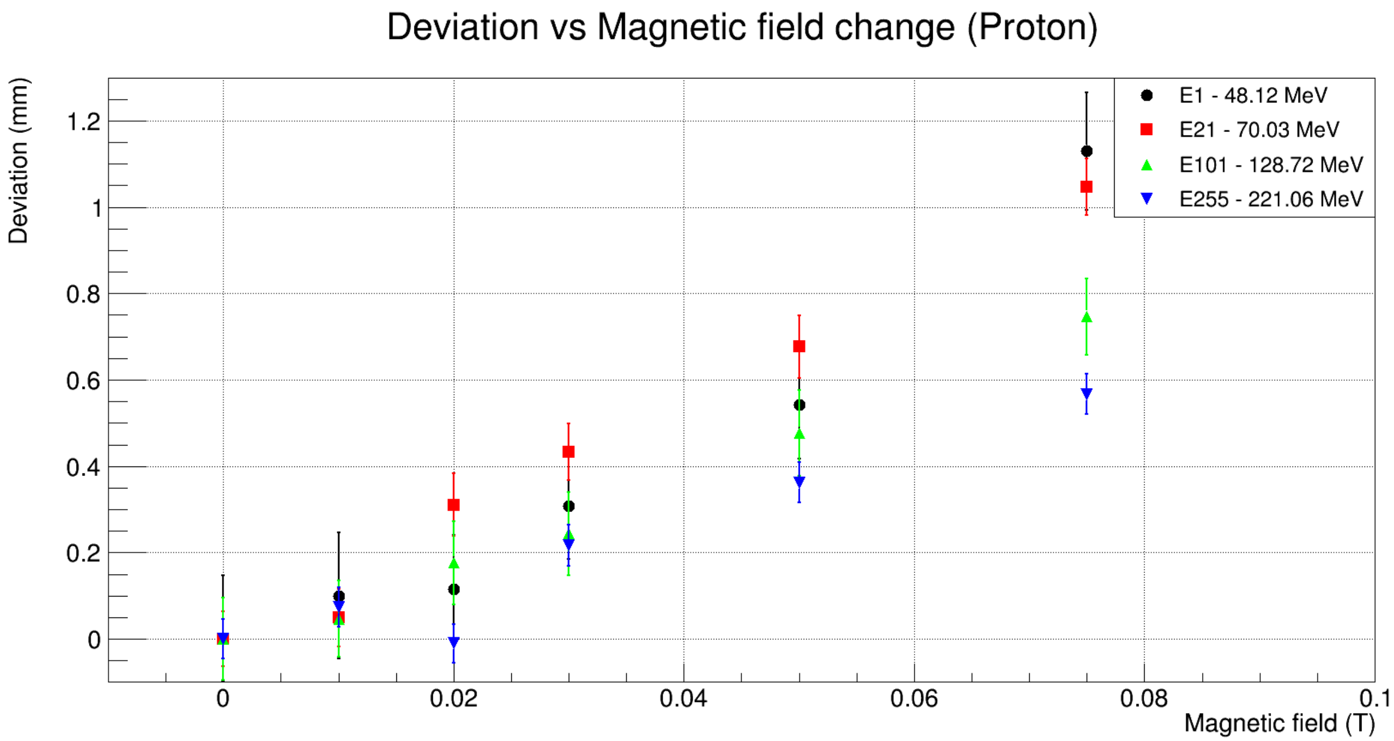
$$D_{ev} \approx \frac{qBD^2}{2\gamma m_0 v}$$

$$Dev \propto \frac{1}{momentum}$$

We use the maximum flux density as the constant magnetic field during the whole path inside the Helmholtz coil

Experimental Results

- We can only calculate their statistical result (average position of all frames)
- Beams are not ideal beams: for the same position setting but **different energy or for different spills**, the **real beam position might be different →** need to subtract the offset
- We have already improved before that : the detector's position resolution is better than **0.05 mm** for this intensity
- Very precis value to be measured

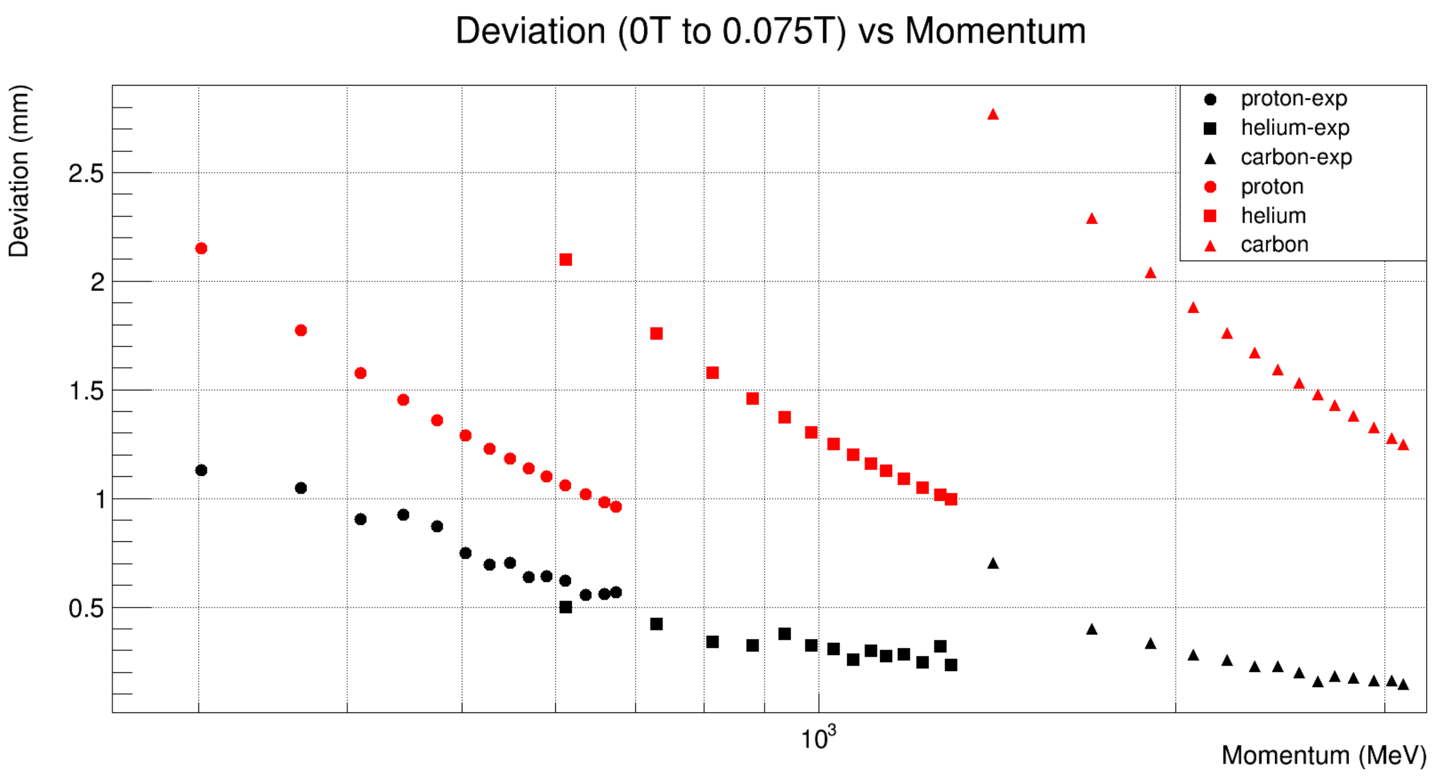


Results and deductions

Red points from calculation for a constant magnetic field

→ Expected to be too large

→ Calculations need to be refined using magnetic field maps



Conclusion and Future work

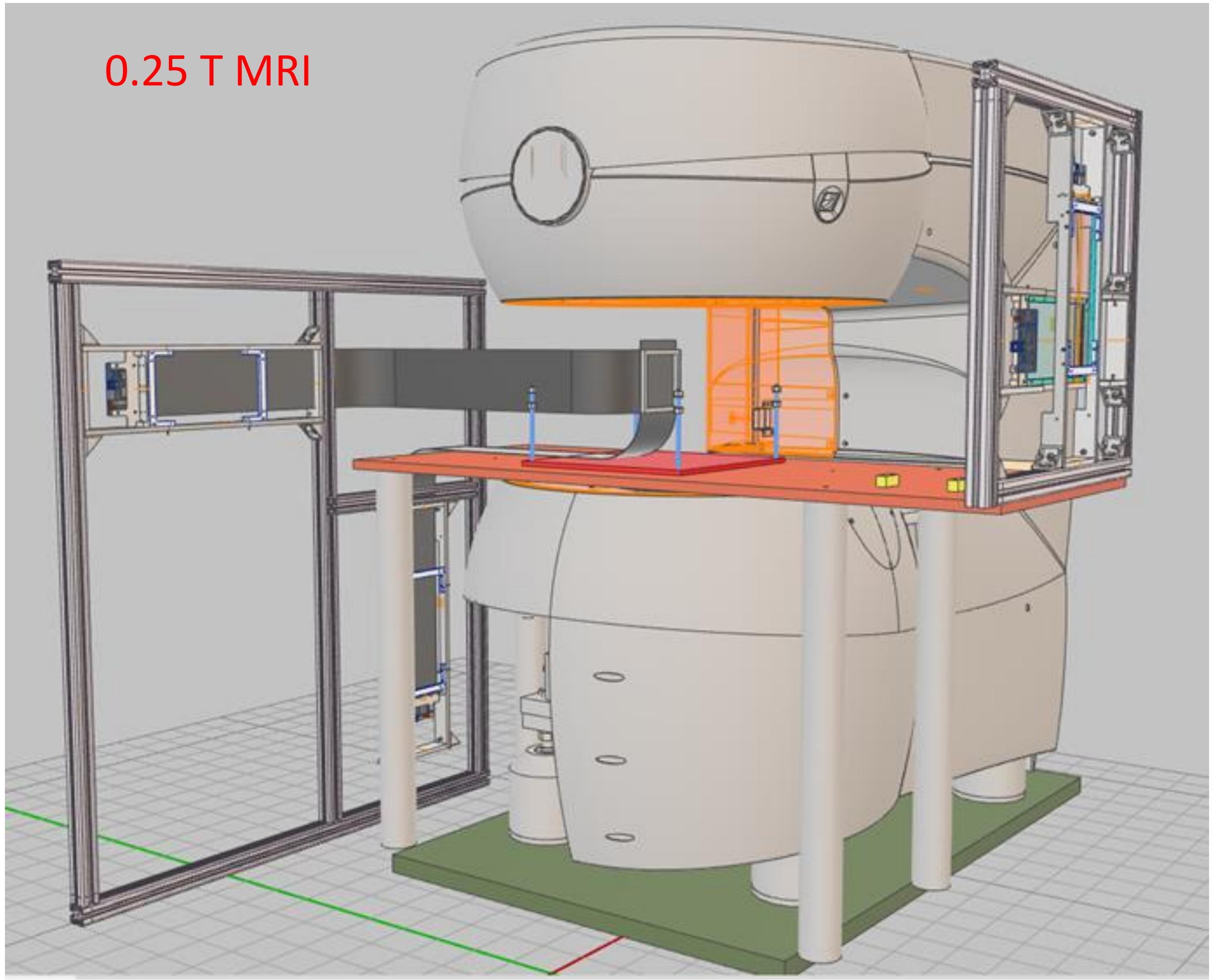
The magnetic field effect the electronics of the beam-on profile detector →not clear how magnetic field affects electronics

Complementary work about magnetic field will be further developed

In the practical situation, the electronics are placed outside of the magnetic field (less flux density than this situation)

We will test the new version of the detector with the 0.25 T MRI and higher

Improve the reconstruction and calibration process



Reference

[1] Commissioning of the Siemens Beam Application and Monitoring System

[2] T. Hoffmann et al., Beam quality measurements at the synchrotron and HEBT of the heidelberg ion therapy center, 2008 Beam Instrumentation Workshop, BIW 2008

[3] S. Giordanengo et al., Dose Delivery Concept and Instrumentation, CERN Yellow Reports: School Proceedings, doi: 10.23730/CYRSP-2017-001.13

[4] D. Ondreka et al., The heidelberg ION Therapy (HIT) accelerator coming into operation, EPAC 2008 - Contributions to the Proceedings

[5] B.D. Leverington et al., A prototype scintillating fibre beam profile monitor for Ion Therapy beams, Journal of Instrumentation, doi: 10.1088/1748-0221/13/05/P05030

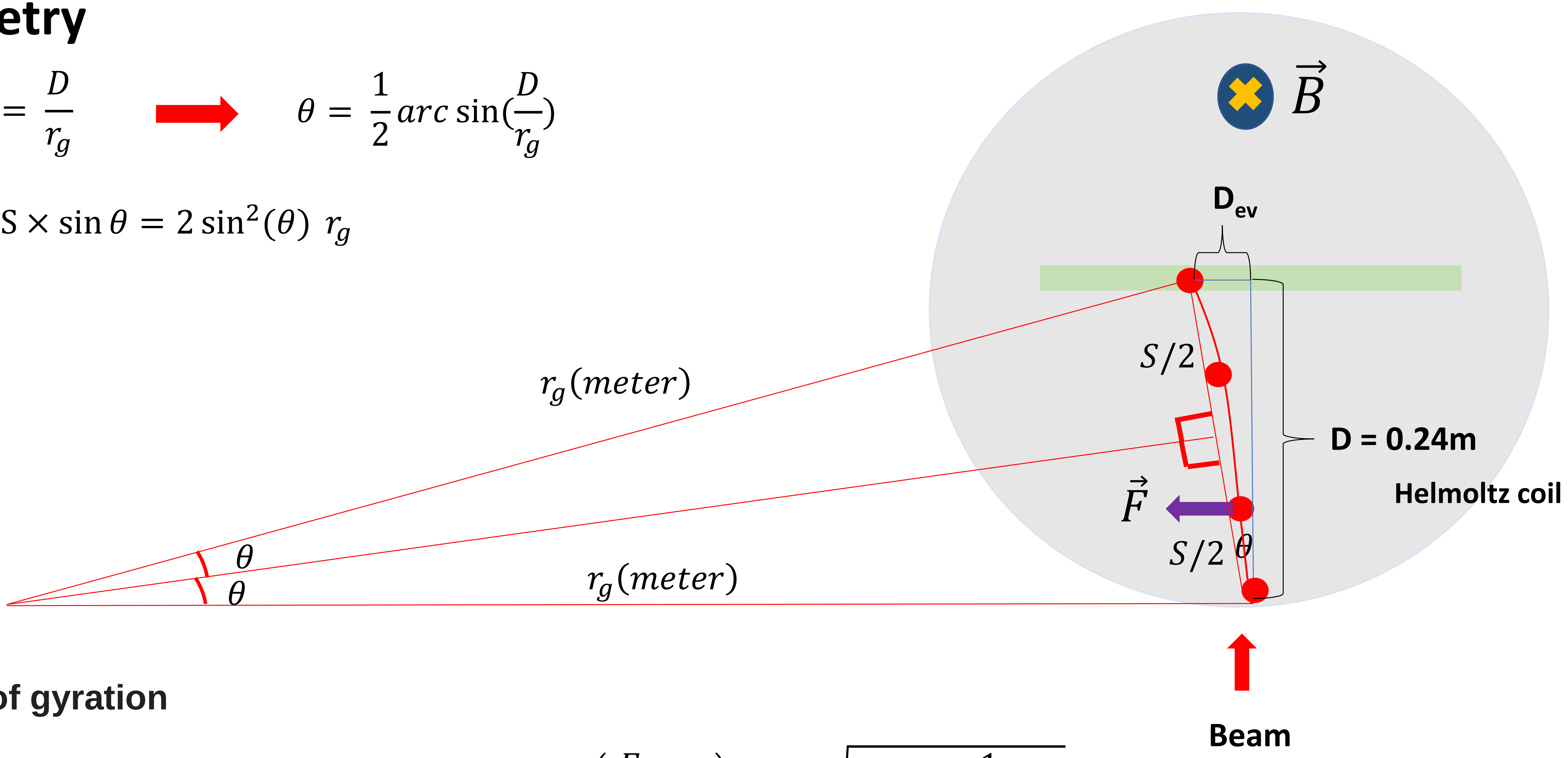
[6] Brian C. Baumann et al., Comparative Effectiveness of Proton vs Photon Therapy as Part of Concurrent Chemoradiotherapy for Locally Advanced Cancer, JAMA Oncol. 2020;6(2):237-246. doi:10.1001/jamaoncol.2019.4889

Thank you for your attention

Geometry

$$\sin 2\theta = \frac{D}{r_g} \quad \Rightarrow \quad \theta = \frac{1}{2} arc\sin(\frac{D}{r_g})$$

$$D_{ev} = S \times \sin\theta = 2\sin^2(\theta)\ r_g$$



Radius of gyration

$$r_g(meter) = 3.3\ \times \frac{[\gamma m_0 c^2(GeV)][v_\perp(c)]}{[|q|(e)][B(Tesla)]} = 3.3 \times \frac{\left(\frac{E}{m_0}+1\right) m_0 \times \sqrt{1 - \frac{1}{(1+\frac{E}{m_0})^2}}}{|q| \times B}$$

Calculate in Relativistic

- **Suppose the beams are ideal beams**
- **Suppose the beam propagate in vacuum**
- **Suppose magnetic field is constant (using the maximum flux density across the inner path of the Helmholtz coil)**

Kinetic energy

$$E = (\gamma - 1)m_0 \Rightarrow \gamma = \frac{E}{m_0} + 1 \Rightarrow 1 - \frac{v^2}{c^2} = \frac{1}{(1+\frac{E}{m_0})^2}$$

$$\Rightarrow v_\perp = c * \sqrt{1 - \frac{1}{(1+\frac{E}{m_0})^2}}$$

	m_0(MeV)	m_0(kg)	q(C)
Proton	938	$1.67*10^{-27}$	1*e
Carbon	938*12	$1.67*10^{-27}*12$	6*e
Helium	938*4	$1.67*10^{-27}*4$	2*e

$$r_g(meter) = 3.3 \times \frac{\left(\frac{E}{m_0}+1\right) m_0 \times \sqrt{1 - \frac{1}{(1+\frac{E}{m_0})^2}}}{|q| \times B}$$

D = 0.24 m

$$\theta = \frac{1}{2} arc\sin(\frac{D}{r_g})$$

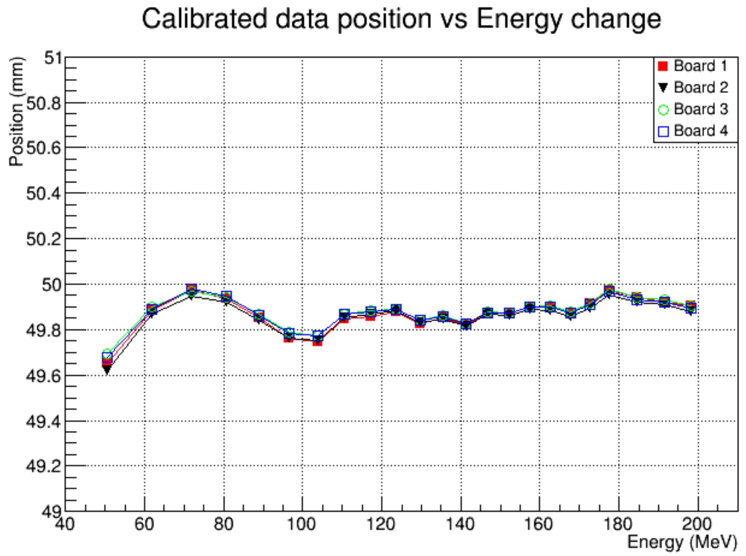
Drifting path: $D_{ev} = \mathrm{S} \times \sin\theta = 2\sin^2(\theta)\ r_g$

The energy scan

- 255 energy settings to chose for each ions
- Each energy have its own focus setting (6 to chose) →several focus but normally we use the **F1** as the setting focus
- For same position in beam plan, different energies have the slightly different position shift

Proton from 48.12 MeV to 221.06 MeV
Helium from 88.8 MeV to 430 MeV
Carbon from 50.57 MeV to 220.51 MeV

For beam plan, we chose **14 energies** and make the energy scan



For proton (energy unit: MeV):

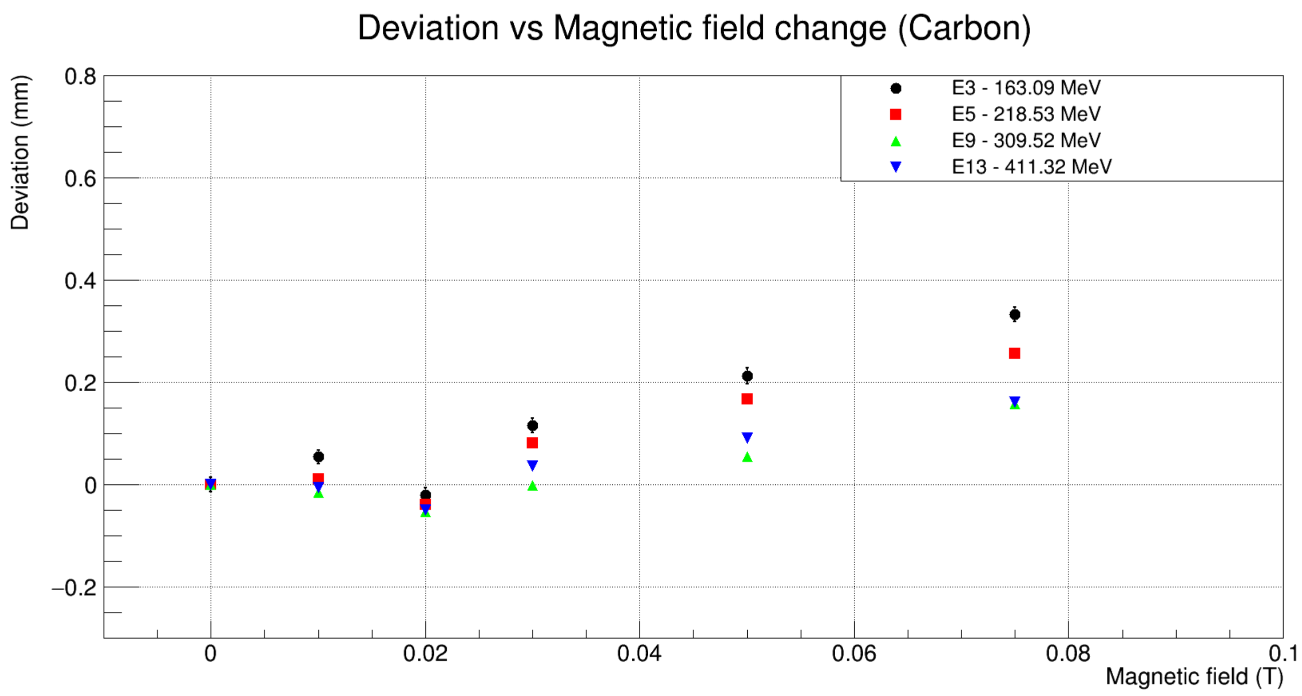
E1	E21	E41	E61	E81	E101	E121	E141	E161	E181	E201	E221	E241	E255
48.12	70.03	87.53	102.61	116.20	128.72	140.41	151.50	162.21	172.62	184.81	198.76	212.06	221.06

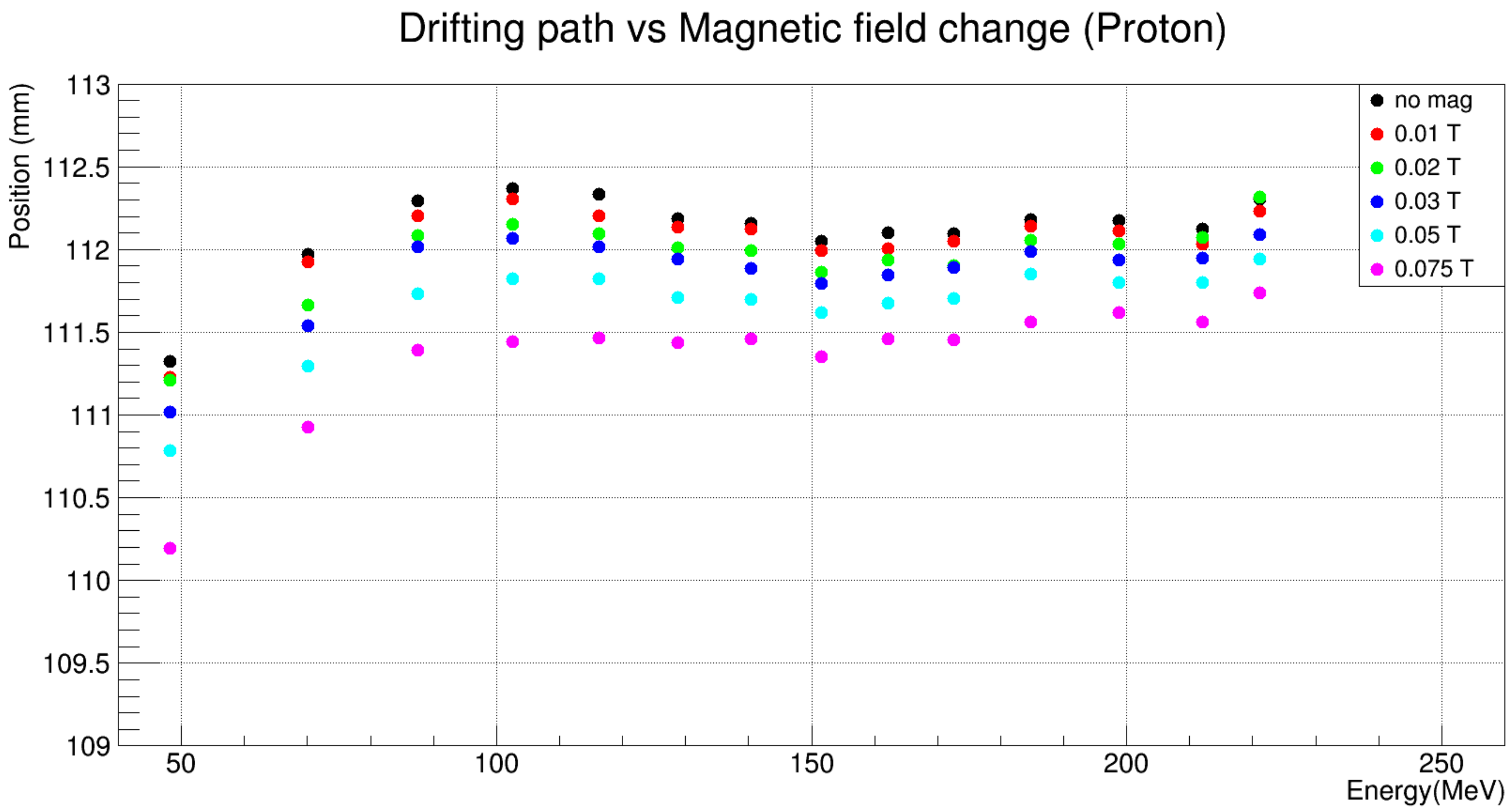
For carbon(energy unit: MeV):

E1	E21	E41	E61	E81	E101	E121	E141	E161	E181	E201	E221	E241	E255
88.83	129.79	163.09	192.09	218.53	243.03	266.08	288.10	309.52	330.48	355.22	383.78	411.32	430.10

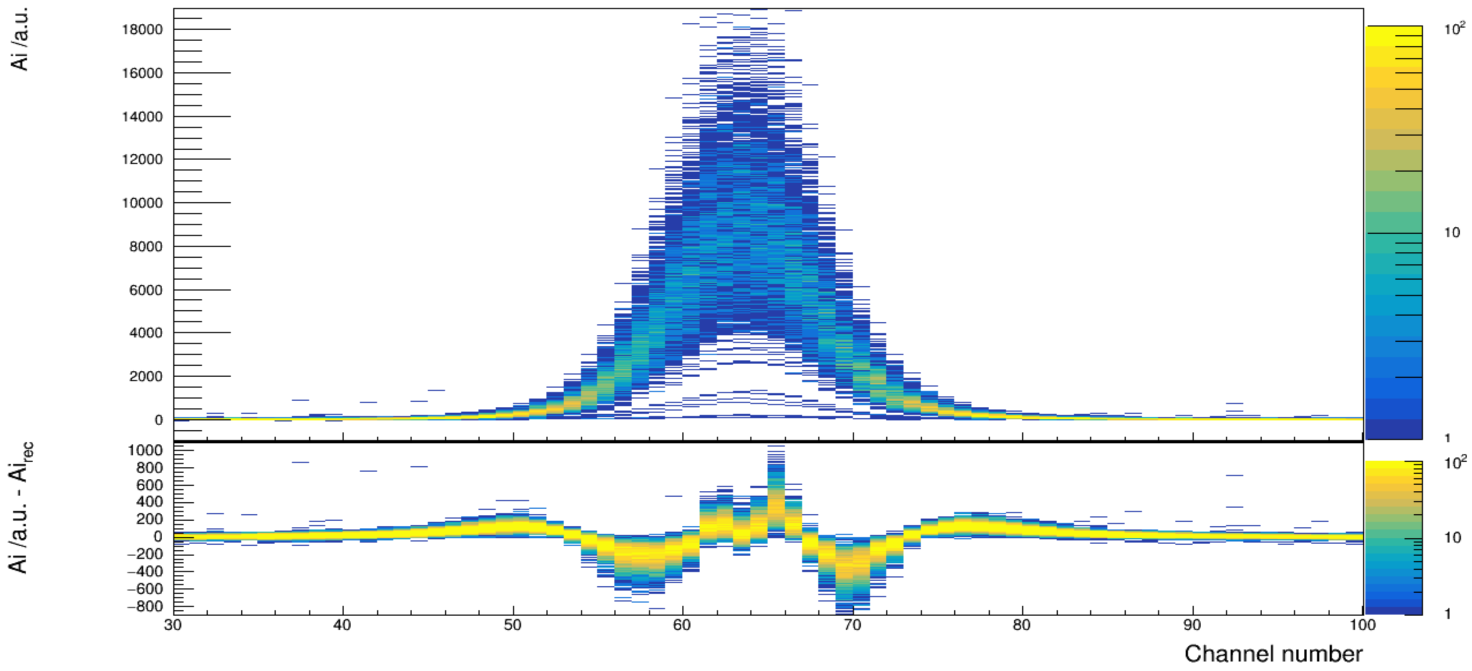
For helium(energy unit: MeV):

E1	E21	E41	E61	E81	E101	E121	E141	E161	E181	E201	E221	E241	E255
50.57	71.73	88.85	103.76	117.23	129.64	141.27	152.26	162.73	172.77	184.56	198.36	211.57	220.51


Deviation vs Magnetic field change (Carbon)
Deviation (mm)
0.8
0.6
0.4
0.2
0
−0.2
0
0.02
0.04
0.06
0.08
0.1
Magnetic field (T)
E3 - 163.09 MeV
E5 - 218.53 MeV
E9 - 309.52 MeV
E13 - 411.32 MeV

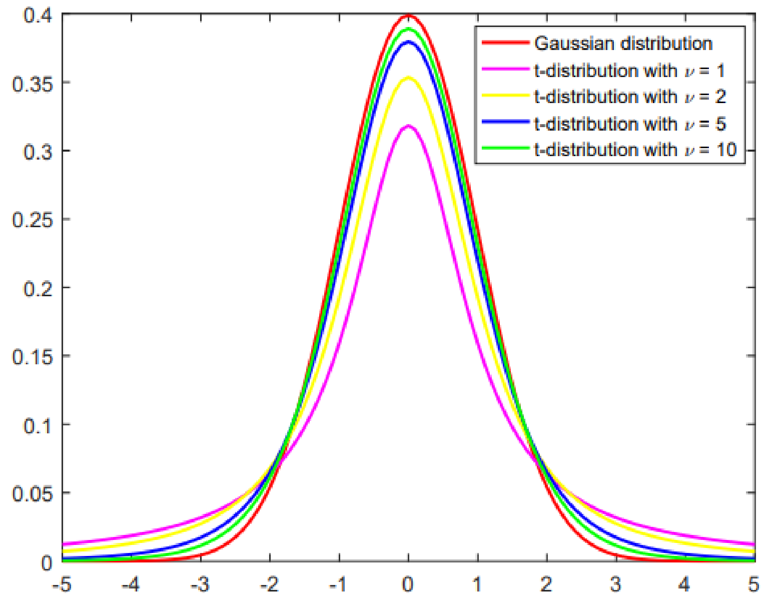

Drifting path vs Magnetic field change (Proton)
Position (mm)
113
112.5
112
111.5
111
110.5
110
109.5
109
50
100
150
200
250
Energy(MeV)
no mag
0.01 T
0.02 T
0.03 T
0.05 T
0.075 T

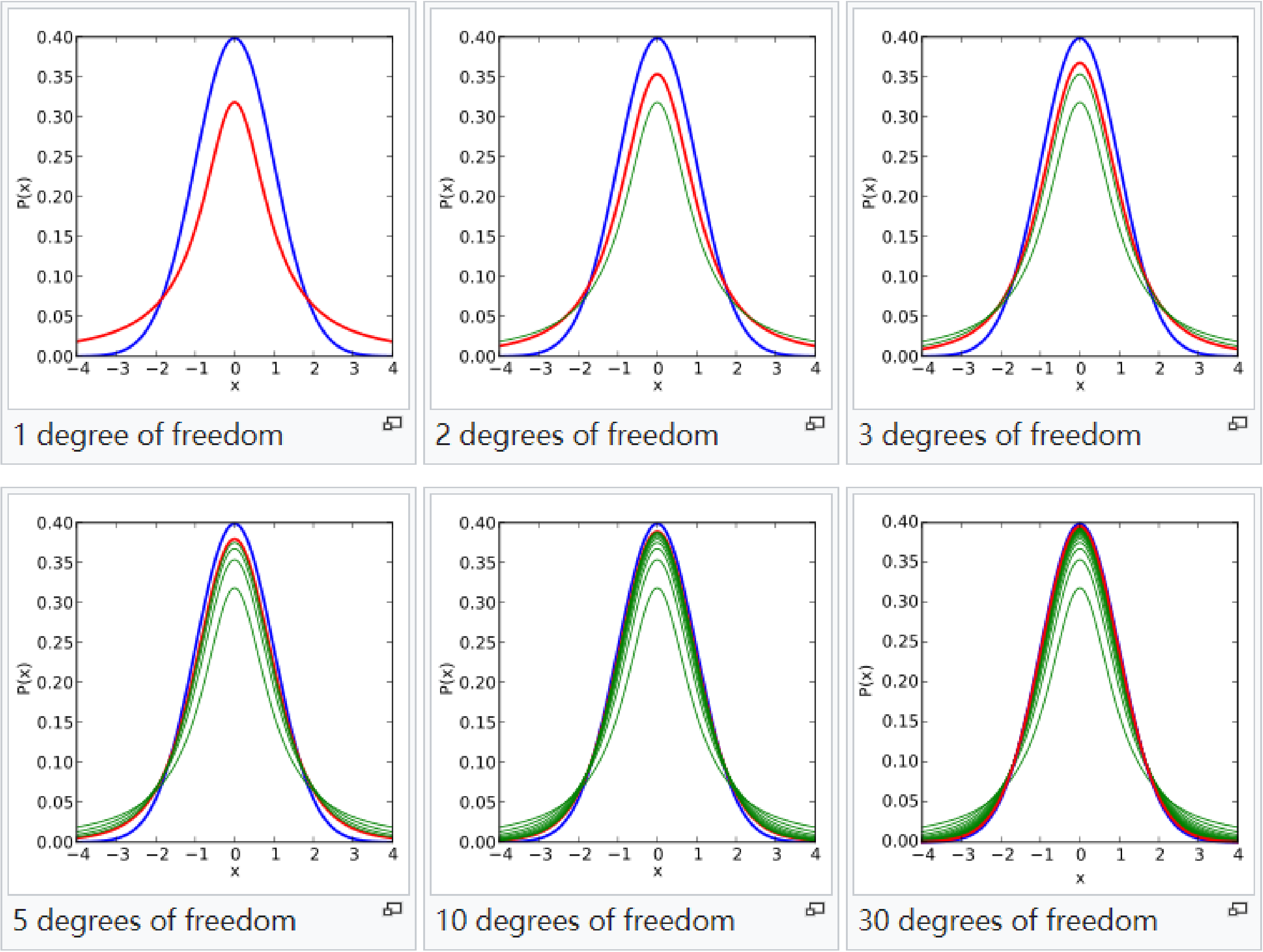
The beam shape



Student T distribution

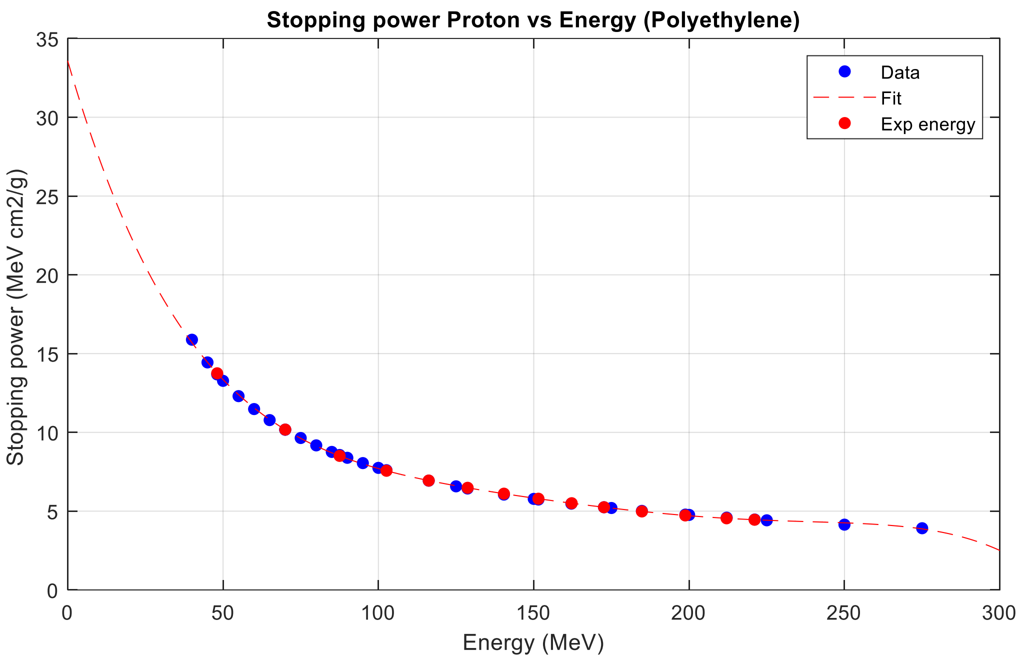
$$f(x) = \frac{\Gamma((\nu+1)/2)}{\sqrt{\nu\pi}\,\Gamma(\nu/2)(1+x^2/\nu)^{(\nu+1)/2}}$$

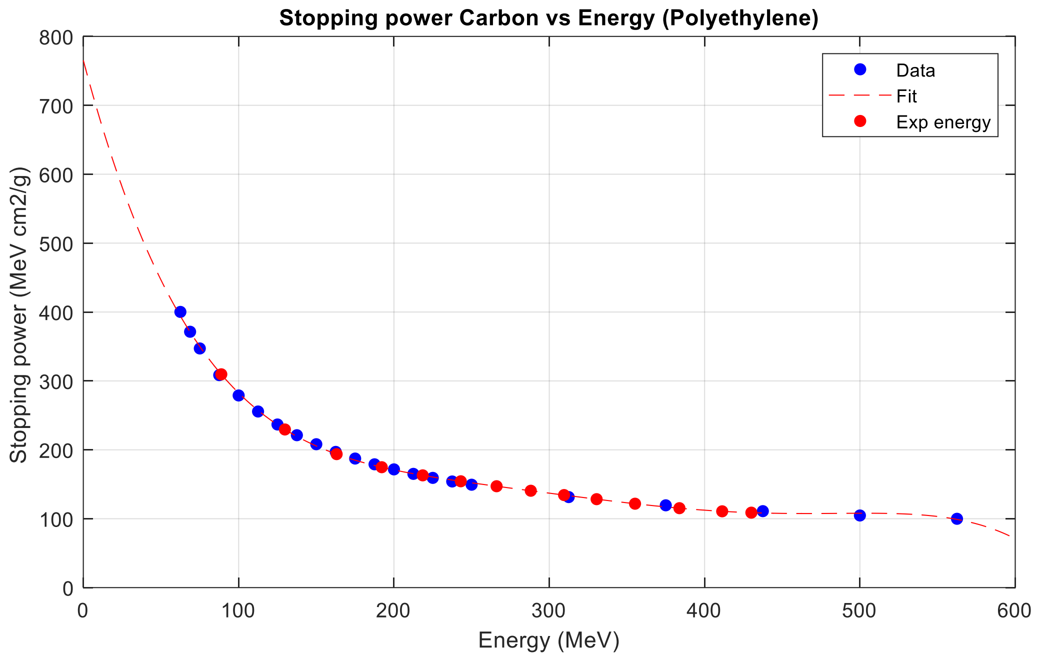


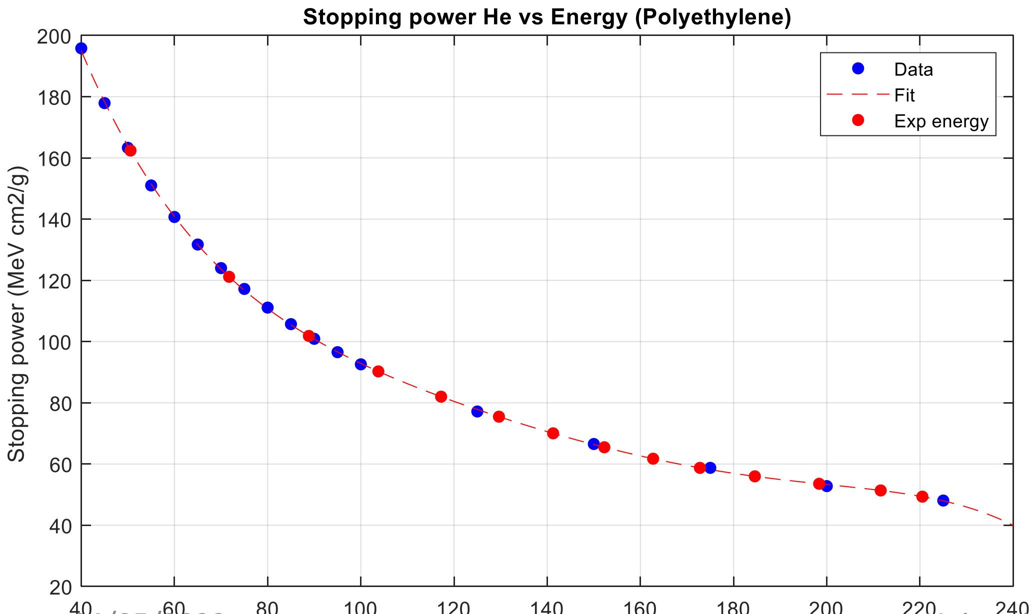


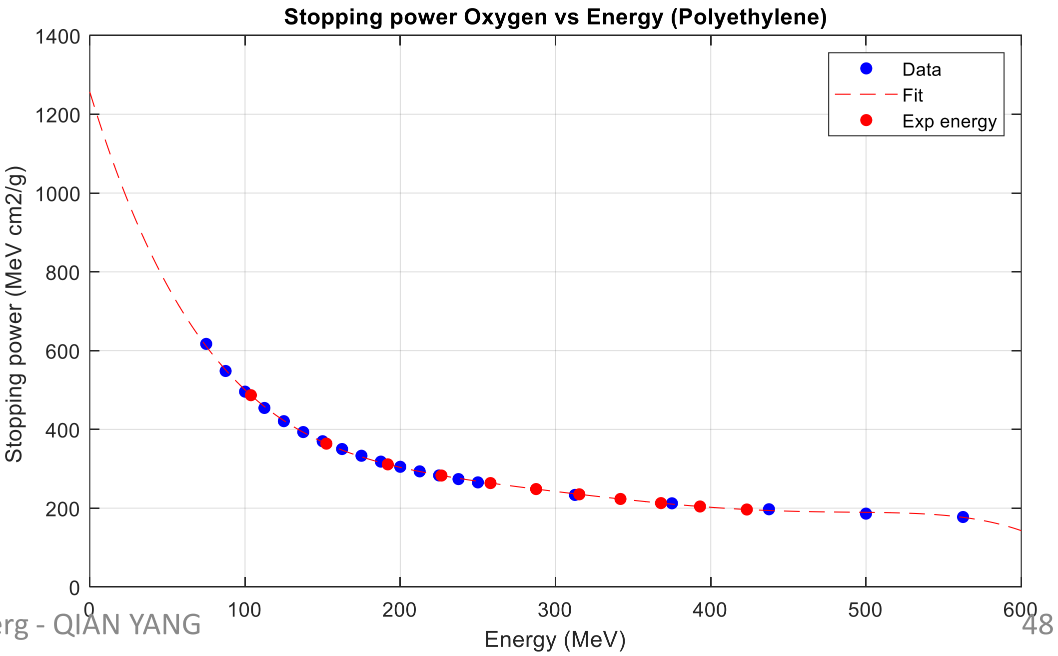
1 degree of freedom | 2 degrees of freedom | 3 degrees of freedom

5 degrees of freedom | 10 degrees of freedom | 30 degrees of freedom

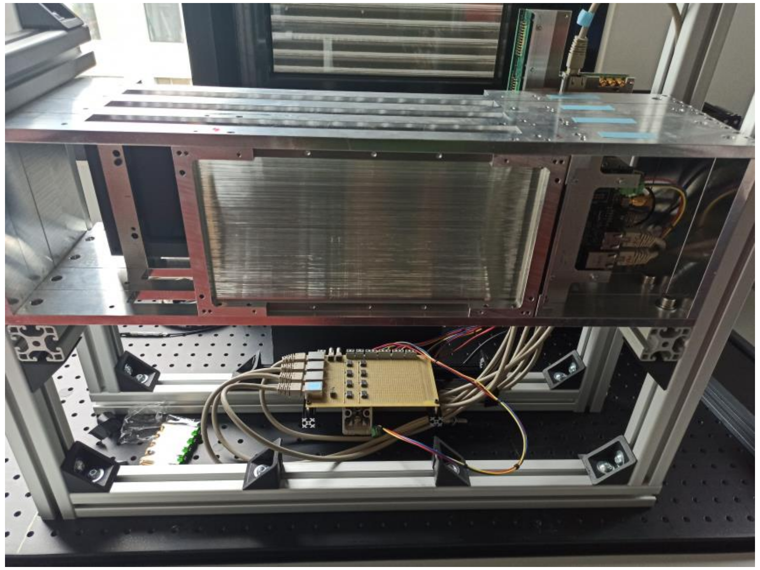

Stopping power Proton vs Energy (Polyethylene)
Stopping power (MeV cm2/g)
Energy (MeV)
Data
Fit
Exp energy


Stopping power Carbon vs Energy (Polyethylene)
Stopping power (MeV cm2/g)
Energy (MeV)
Data
Fit
Exp energy


Stopping power He vs Energy (Polyethylene)
Stopping power (MeV cm2/g)
Energy (MeV)
Data
Fit
Exp energy


Stopping power Oxygen vs Energy (Polyethylene)
Stopping power (MeV cm2/g)
Energy (MeV)
Data
Fit
Exp energy

4 boards are in the same direction → horizontal

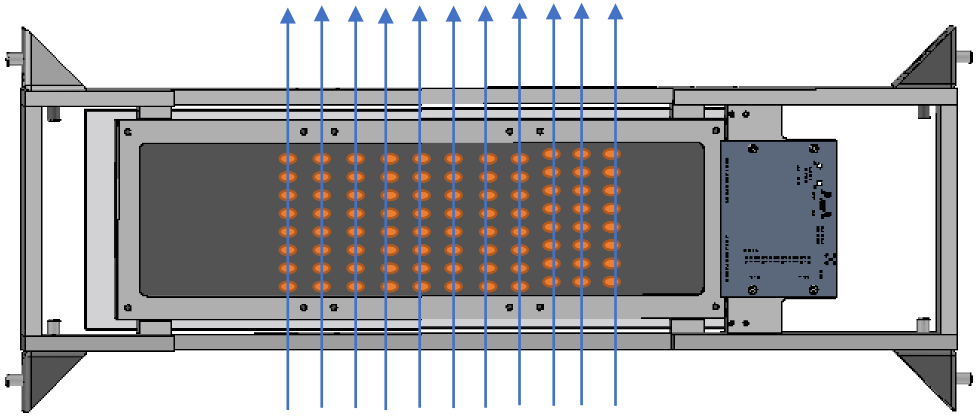


Board 0 : two layers fibre with glue / 400mm /no mirror at the end

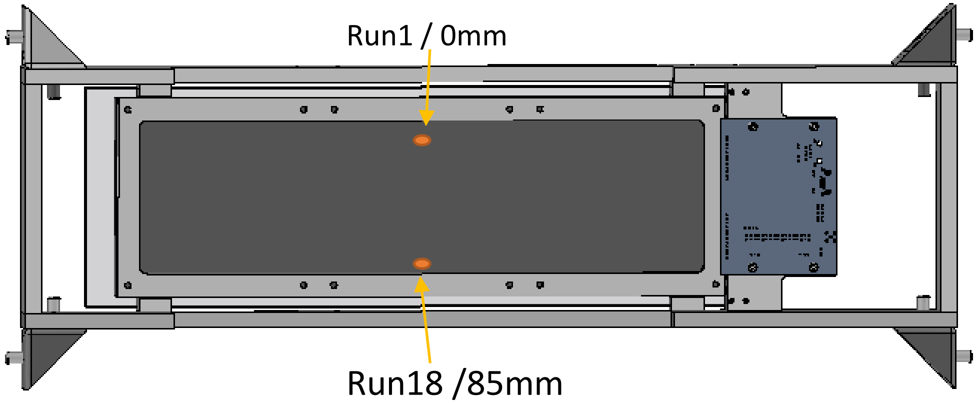
Board 1 : two layers fibre with glue /400mm/ radiation damage/mirror

Board 2 : two layers fibre without glue/ 300mm/mirror

Board 3 : two layers fibre without glue/ 300mm/mirror



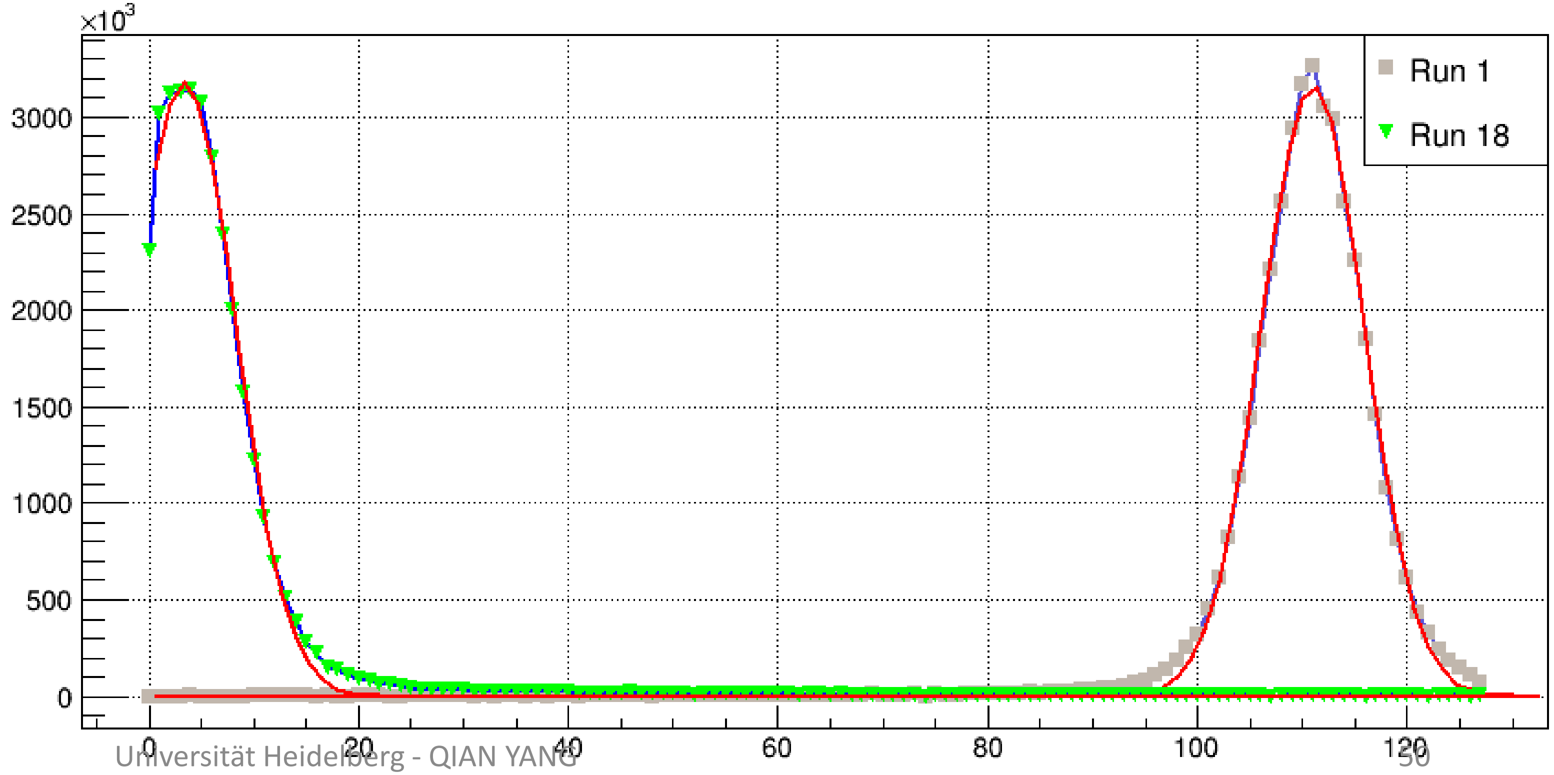
Method 1 Step 1



- Gaussian fit the run 1 and run18
- Run1 : 0 mm (HIT)
- Run 18: 85 mm (HIT)

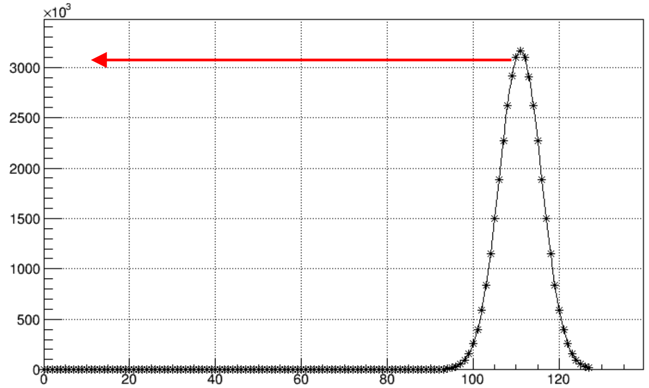
- Find peak position, peak amplitude and sigma

```
run1 mean value: 111
run18 mean value: 3.36785
run1 peak value: 3.1609e+06
run18 peak value: 3.18349e+06
run1 sigma value: 4.91876
run18 sigma value: 4.90804
```

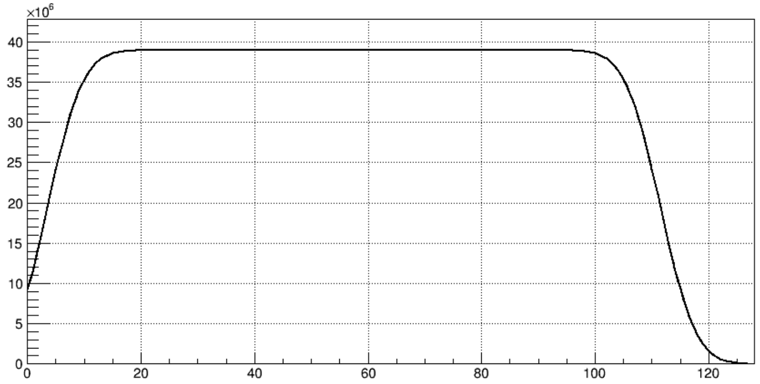


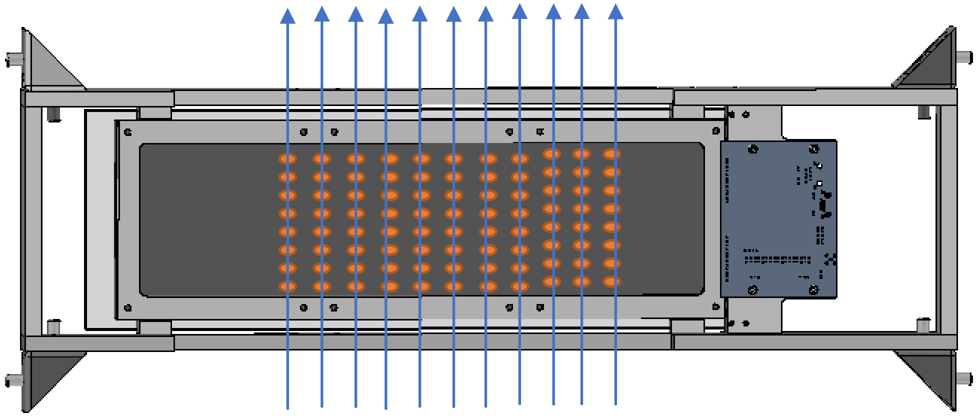
Step 2 The added profile

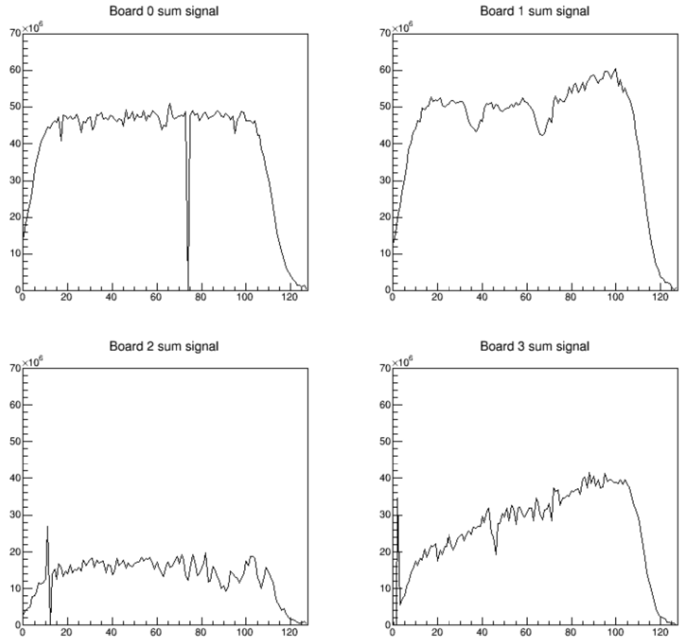
- Create a vector of gaussian of run 1
- Move it to the 85 mm place
- Move the vector and add the distribution together with **1 channel step**
- (need to chose another gaussian later)



The ideal profile(use as reference)

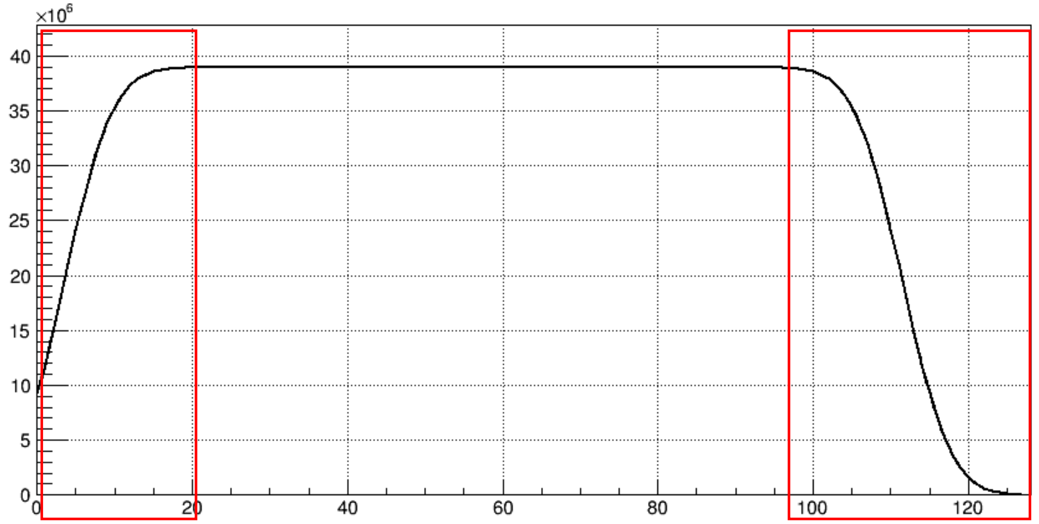


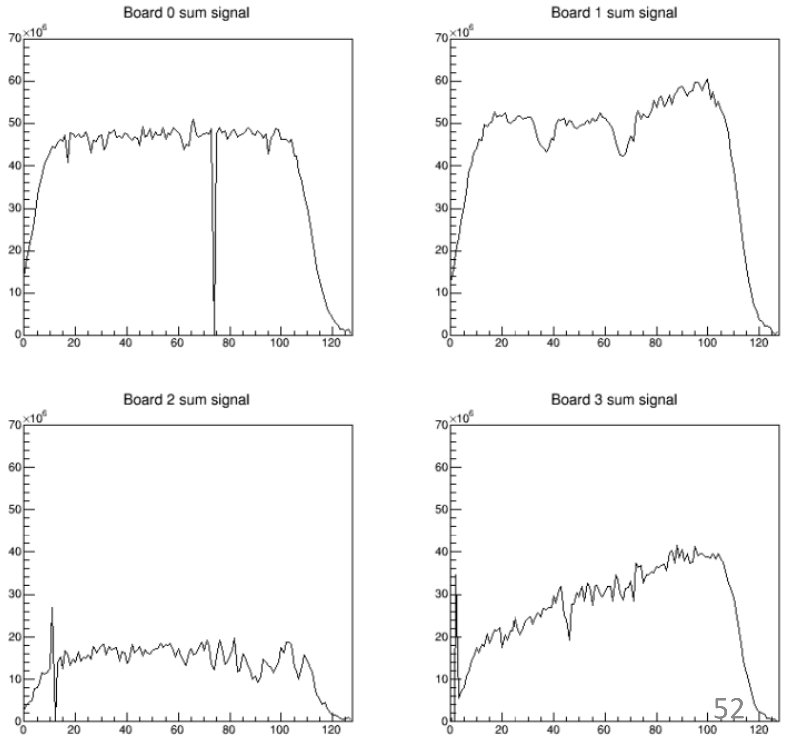


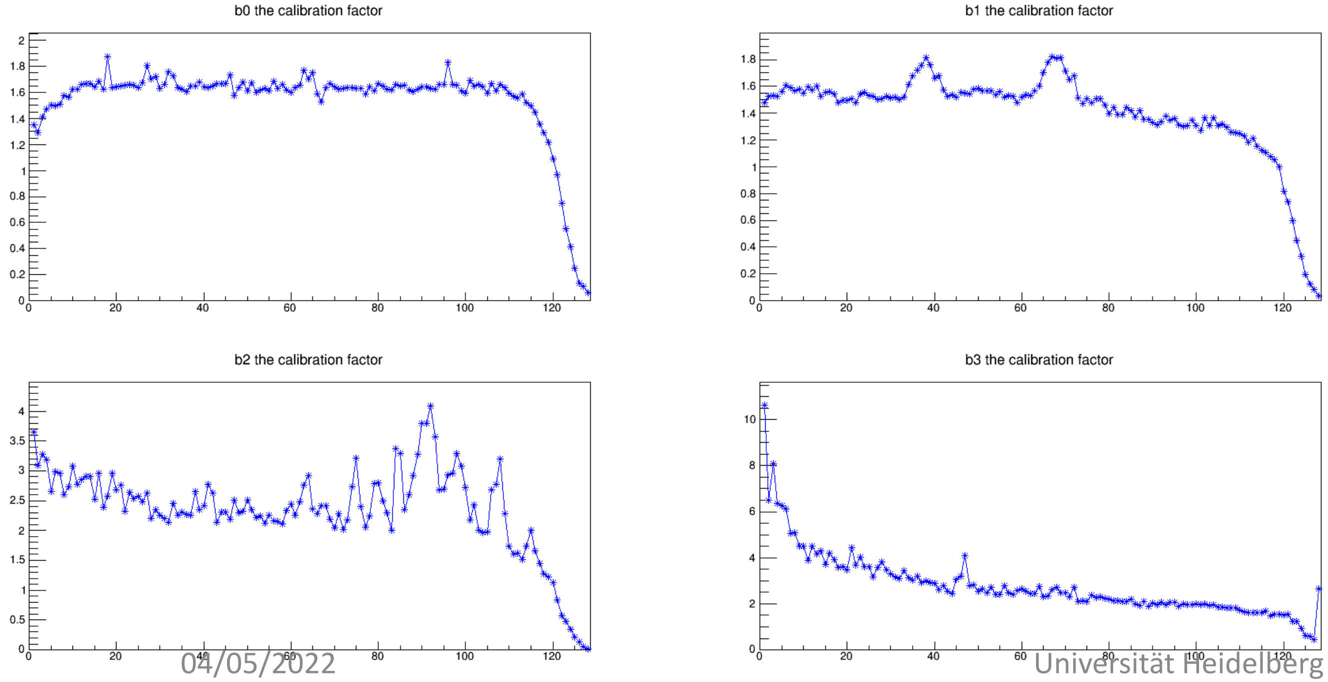


Step 3 calibration

- Due the limit of the scan, after 115 - 128 is not well corrected
- The next experiment the scan should cover the plan(!)







Données : $(x_1, f_1), (x_2, f_2), \ldots, (x_k, f_k), \ldots, (x_n, f_n)$

- Calcul des S_k :

$$\begin{cases} S_1 = 0 \\ S_k = S_{k-1} + \frac{1}{2}(f_k + f_{k-1})(x_k - x_{k-1}) \qquad k = 2 \to n \end{cases}$$

- Calcul des T_k :

$$\begin{cases} T_1 = 0 \\ T_k = T_{k-1} + \frac{1}{2}(x_k\ f_k + x_{k-1}\ f_{k-1})(x_k - x_{k-1}) \qquad k = 2 \to n \end{cases}$$

-Calcul de : $\sum (S_k)^2, \sum S_k T_k, \sum (T_k)^2,$
$\sum (y_k - y_1) S_k, \sum (y_k - y_1) T_k$

- Calcul de A_1 et B_1 :

$$\begin{pmatrix} A_1 \\ B_1 \end{pmatrix} = \begin{pmatrix} \sum (S_k)^2 & \sum S_k T_k \\ \sum S_k T_k & \sum (T_k)^2 \end{pmatrix}^{-1} \begin{pmatrix} \sum (y_k - y_1) S_k \\ \sum (y_k - y_1) T_k \end{pmatrix}$$

- Calcul de σ_1 et μ_1 : $\sigma_1 = -\frac{1}{B_1}\sqrt{\frac{2}{\pi}}$; $\mu_1 = -\frac{A_1}{B_1}$

Résultat : σ_1 et μ_1 sont les valeurs approchées de σ et μ

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2 \right)$$

$$\int_{x_1}^{x} (t-\mu) f(t)\, dt = -\sqrt{\frac{\pi}{2}}\, \sigma \left(f(x) - f(x_1) \right)$$

$$\begin{cases} f(x) - f(x_1) = A \int_{x_1}^{x} f(t)\, dt + B \int_{x_1}^{x} t\, f(t)\, dt \\ \text{avec : } A = \frac{\mu}{\sigma}\sqrt{\frac{2}{\pi}} \quad \text{et} \quad B = -\frac{1}{\sigma}\sqrt{\frac{2}{\pi}} \end{cases}$$

$$\begin{cases} S_1 = 0 \\ S_k = S_{k-1} + \frac{1}{2}(f_k + f_{k-1})(x_k - x_{k-1}) \qquad k = 2 \to n \end{cases}$$

$$\begin{cases} T_1 = 0 \\ T_k = T_{k-1} + \frac{1}{2}(x_k\ f_k + x_{k-1}\ f_{k-1})(x_k - x_{k-1}) \qquad k = 2 \to n \end{cases}$$

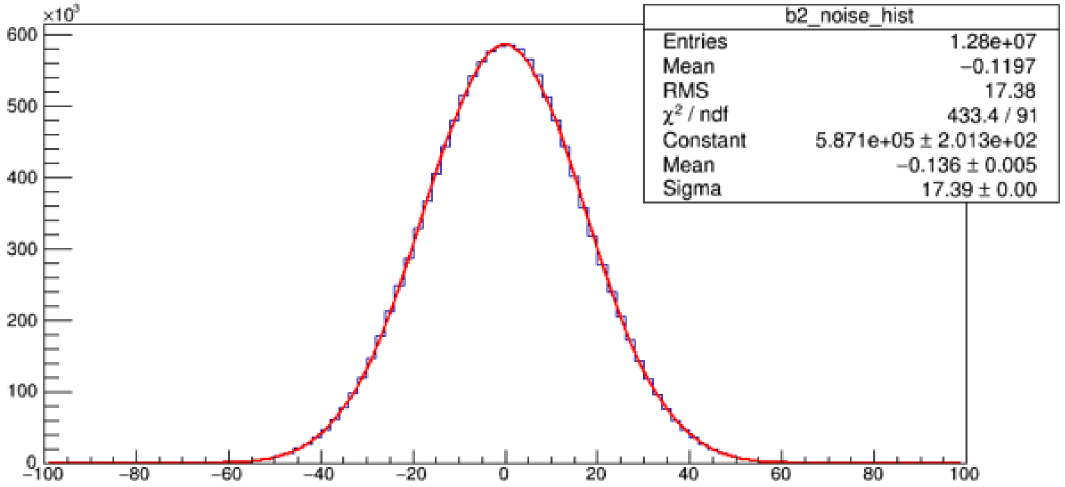
$$\sum_{k=1}^{n} \varepsilon_k^2 = \sum_{k=1}^{n} \left(-(f_k - f_1) + A\, S_k + B\, T_k \right)^2$$

$$\begin{pmatrix} A_1 \\ B_1 \end{pmatrix} = \begin{pmatrix} \sum (S_k)^2 & \sum S_k T_k \\ \sum S_k T_k & \sum (T_k)^2 \end{pmatrix}^{-1} \begin{pmatrix} \sum (y_k - y_1) S_k \\ \sum (y_k - y_1) T_k \end{pmatrix}$$

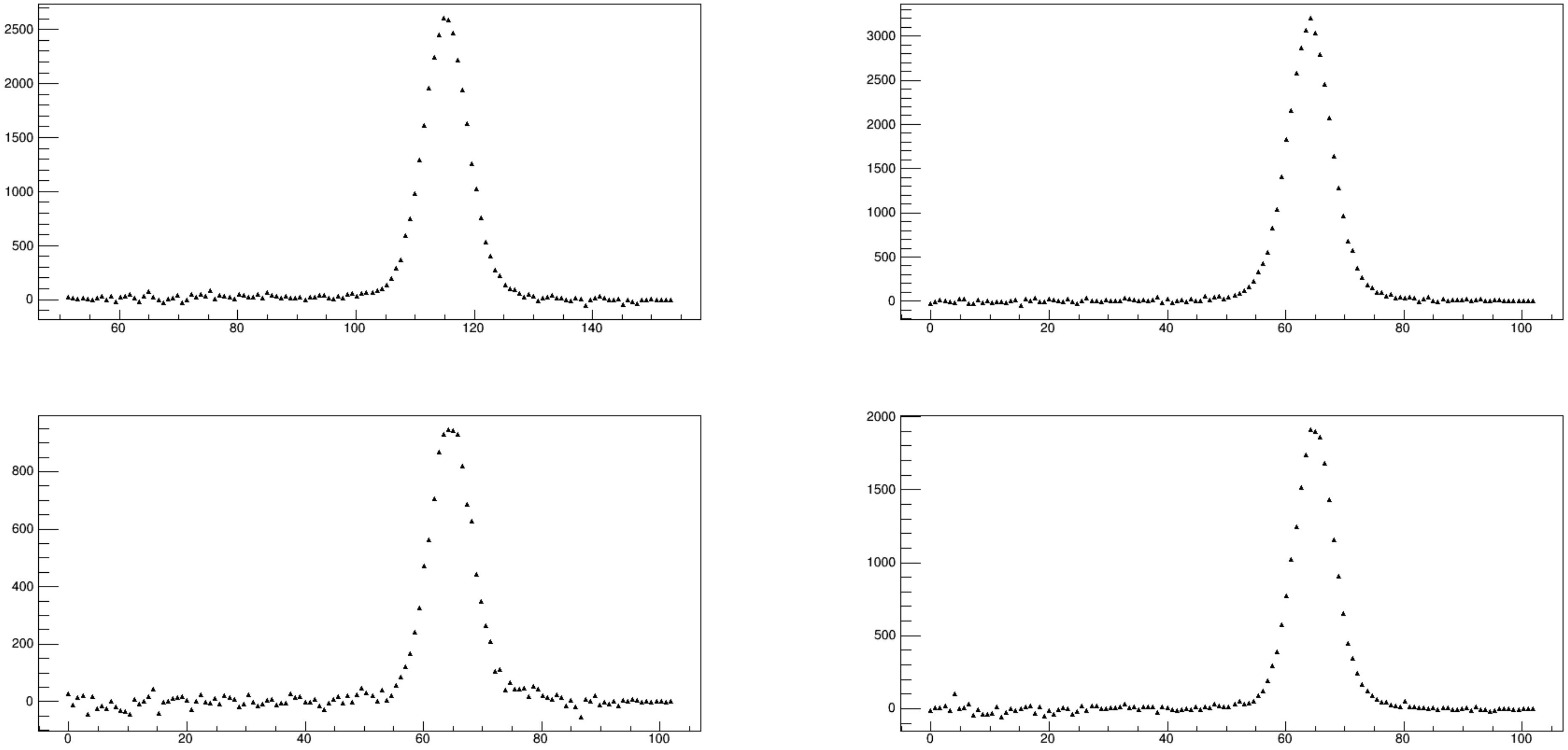
$$\sigma_1 = -\frac{1}{B_1}\sqrt{\frac{2}{\pi}} \quad ; \quad \mu_1 = -\frac{A_1}{B_1}$$

SNR

- SNR = Peak value (amplitude) / noise distribution FWHM
- FWHM : 2.355 * sigma of gaussian distribution



	begin	end	frame	particle/1000000	intensity
i1	128242	153905	25663	325	126,6414683
i2	189153	214458	25305	520	205,4929856
i3	249174	281067	31893	780	244,5677735
i4	316100	350488	34388	1040	302,4310806
i5	385081	420089	35008	1560	445,6124314
i6	454989	490299	35310	2080	589,0682526
i7	524963	560437	35474	3120	879,517393
i8	594884	630677	35793	5200	1452,798033
i9	664878	700694	35816	8320	2322,984141


0 500 1000 1500 2000 2500
60 80 100 120 140
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