

Application of the GEMPix Detector in Radiation Protection and Particle Therapy

Von der Fakultät für Mathematik, Informatik und Naturwissenschaften der RWTH
Aachen University zur Erlangung des akademischen Grades eines Doktors der
Naturwissenschaften genehmigte Dissertation

vorgelegt von

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Tag der mündlichen Prüfung: 03.07.2019

Diese Dissertation ist auf den Internetseiten der Universitätsbibliothek online
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Abstract

The GEMPix is a small gaseous detector with a highly pixelated readout. It consists of a sensitive volume ($2.8 \times 2.8 \times 0.3 \text{ cm}^3$ or $2.8 \times 2.8 \times 1.2 \text{ cm}^3$) to detect ionising radiation, three Gas Electron Multipliers (GEMs) for signal amplification and four Timepix Application-Specific Integrated Circuits (ASICs) with 262,144 pixels of $55 \times 55 \mu\text{m}^2$ area each for readout. It is continuously flushed with Ar:CO₂:CF₄ (45:15:40) gas. Before applications are investigated, a detailed detector characterisation is performed and results such as gain scans are reported. Also, a correction necessary for a stable detector response despite changes of temperature, pressure and humidity is developed. The GEMPix has found several applications two of which are investigated in this thesis.

A proof-of-concept for measurements of the ⁵⁵Fe content in activated steel samples of radioactive waste is reported. ⁵⁵Fe is an important radionuclide in the elimination procedures of waste produced at facilities like the European Organization for Nuclear Research (CERN) housing accelerator based experiments. Forty-five samples are used to calibrate the GEMPix counts to specific activity. The detection limit and the sensitivity to the Swiss clearance limit are investigated. The GEMPix is potentially sensitive to the clearance limit but a detailed uncertainty study will be needed before a potential operational phase. Liquid radioactive sources could improve the calibration.

3D measurements of the energy deposited by a hadron beam in a water phantom represent an important step towards a possible use of the GEMPix for quality assurance in hadron therapy, one of the main cancer treatment modalities. An integrated system is developed and consists of a commercial water phantom with a motorised positioning system, a reference ionisation chamber and the GEMPix. Bragg curves obtained with this system match Monte Carlo simulations with the Fluctuating Cascade (FLUKA) code within 10% for most data points for carbon ions of three different clinical energies. For this application, a larger sensitive area matching the typical maximum radiation field size of $20 \times 20 \text{ cm}^2$ is necessary. Therefore solutions based on the Timepix ASIC and on other readout principles such as the detection of optical photons produced in the GEMs are currently under investigation.

Zusammenfassung

Der GEMPix ist ein kleiner Gasdetektor mit hoher Ortsauflösung. Er besteht aus einem Detektionsvolumen ($2.8 \times 2.8 \times 0.3 \text{ cm}^3$ oder $2.8 \times 2.8 \times 1.2 \text{ cm}^3$) zur Messung ionisierender Strahlung, drei GEMs (Gaselektronenvervielfacher) zur Signalverstärkung und vier Timepix ASICs (anwendungsspezifische integrierte Schaltung) mit 262,144 jeweils $55 \times 55 \mu\text{m}^2$ großen Pixeln. Der Detektor wird kontinuierlich mit $\text{Ar:CO}_2\text{:CF}_4$ (45:15:40) Gas durchspült. Vor der Untersuchung verschiedener Anwendungen wird eine detaillierte Detektorcharakterisierung durchgeführt, deren Ergebnisse vorgestellt werden – zum Beispiel Messungen mit verschiedenen Verstärkungsfaktoren. Außerdem wird eine Korrekturfunktion entwickelt, die für ein stabiles Detektorverhalten bei sich verändernden Temperatur-, Druck- und Luftfeuchtigkeitswerten nötig ist. Zwei der zahlreichen bekannten Anwendungen des GEMPix werden in dieser Arbeit detailliert untersucht.

Zunächst wird ein Machbarkeitsnachweis für Messungen des ^{55}Fe -Gehalts in aktivierten Stahlproben aus radioaktivem Abfall erarbeitet. ^{55}Fe ist ein wichtiges Radionuklid im Entsorgungsprozess von Abfall, der an Forschungszentren wie dem CERN (Europäische Organisation für Kernforschung) mit beschleunigerbasierten Experimenten anfällt. Die Umrechnung der GEMPix-Signale in spezifische Aktivität wird durch Messungen mit 45 Proben zur Kalibrierung ermöglicht. Die Nachweisgrenze und die Empfindlichkeit auf den Schweizer Freigabe-Grenzwert werden untersucht. Die Empfindlichkeit ist wahrscheinlich ausreichend, jedoch ist eine detaillierte Untersuchung der Unsicherheiten vor einer Anwendung nötig. Flüssige radioaktive Quellen könnten die Kalibrierung verbessern.

3D-Messungen der Energiedeposition eines Hadronenstrahls in einem Wasserphantom sind ein wichtiger Schritt hin zu einer möglichen Anwendung des GEMPix in der Qualitätssicherung in der Hadronentherapie, einer üblichen Krebstherapie. Messungen werden mit einem hierfür entwickelten System durchgeführt, das aus einem kommerziellen Wasserphantom mit motorisiertem Positionierungssystem, einer Ionisationskammer als Referenzdetektor und dem GEMPix besteht. Die gemessenen Bragg-Kurven stimmen mit Monte Carlo-Simulationen, für die der FLUKA-Code verwendet wird, für die meisten Datenpunkte innerhalb von 10% überein. Verglichen werden Messung und Simulation mit Kohlenstoffionen bei drei verschiedenen Energien. Eine größere Detektionsfläche, angepasst an das typische maximale

Strahlungsfeld von $20 \times 20 \text{ cm}^2$, ist für diese Anwendung nötig. Daher werden zur Zeit Ausleseoptionen basierend auf dem Timepix ASIC und anderen Methoden – wie zum Beispiel der Messung von optischen Photonen, die in den GEMs produziert werden – untersucht.

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1. Introduction

Particle detectors are a fundamental tool in experimental physics for example to reconstruct particle collisions in the Large Hadron Collider (LHC) experiments at the European Organization for Nuclear Research (CERN). There are also several applications outside physics research such as the detection of optical photons in a camera or medical X-ray imaging.

The GEMPix is a small gaseous detector with a highly pixelated readout that was developed in the Radiation Protection Group at CERN in the course of the Marie Curie project ARDENT [1] (2012-2016). Ionising radiation such as X-rays or ions produces electron-ion pairs in the sensitive volume ($2.8 \times 2.8 \times 0.3 \text{ cm}^3$ or $2.8 \times 2.8 \times 1.2 \text{ cm}^3$ depending on the application). The electrons are guided by an electric field towards three Gas Electron Multipliers (GEMs) for signal amplification. Finally they are detected by four Timepix Application-Specific Integrated Circuits (ASICs) with 262,144 pixels of $55 \times 55 \mu\text{m}^2$ area each for readout. The GEMPix is continuously flushed with Ar:CO₂:CF₄ (45:15:40) gas.

Since the GEMPix is able to measure very low energy X-rays down to about 2 keV, it is a good candidate to measure the 5.9 keV X-rays of ⁵⁵Fe. The spatial resolution of the GEMPix enables basic particle identification and therefore suppression of background from other radionuclides such as ⁶⁰Co. Measurements of the ⁵⁵Fe content in radioactive waste are an important issue for facilities like CERN housing accelerator based particle physics experiments: once dismantled the possibly activated material becomes radioactive waste that needs to be treated according to Swiss and French legislation. The radionuclide content has to be characterised following standard waste elimination paths towards clearance or final storage. A big part of the waste is steel and ⁵⁵Fe is likely one of the present radionuclides. The GEMPix could potentially replace the standard measurement – the radiochemical analysis – which is performed by external companies for CERN and takes usually 2 months in total.

Another application of the GEMPix is quality assurance in hadron therapy, one of the main cancer treatment modalities. The irradiation parameters and the patient treatment plan need to be well checked which requires a detector able to measure the energy deposition by a proton or carbon ion beam in a water target. Typically the dose foreseen in a patient treatment plan is measured in a so-called water phan-

tom with an array of ionisation chambers. Only when the measured dose matches the predicted dose within predefined tolerances the treatment plan is verified. The GEMPix can withstand measurements in such a beam and its spatial resolution is better than that of conventional arrays of ionisation chambers.

This thesis seeks to characterise the GEMPix and investigate its capabilities to the two above mentioned applications. Chapter 2 describes the necessary physics background and explains the used software. The GEMPix is introduced and characterised in chapter 3, reporting also on improvements implemented in the detector. The applications to measurements of the ^{55}Fe content in samples of radioactive waste and to the energy deposition measurements for hadron therapy are presented in chapters 4 and 5 respectively. Chapter 6 concludes the thesis and provides an outlook.

2. Background

In this chapter, the physics basics necessary to understand the performed work are briefly explained: the disintegration of nuclei in radioactive decays (section 2.1), the interaction of radiation with matter (section 2.2) and the detection and signal creation process in gaseous detectors (section 2.3). Furthermore, the software used for this work is briefly introduced in section 2.4.

2.1. Radioactive Decays

Unstable nuclei can disintegrate without external influence in radioactive decays. The activity A is a measure for the decay rate [2, p. 47]:

$$A = -\frac{dN}{dt} = \lambda N \quad (2.1)$$

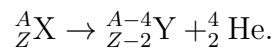
where N is the number of nuclei at time t and λ is the decay constant. The half-life is the time required for the activity to decrease to half of its initial value and is related to the decay constant: $t_{1/2} = \ln(2)/\lambda$. After integration, this equation yields the activity after a certain time:

$$A(t) = \lambda N_0 \exp(-\lambda t). \quad (2.2)$$

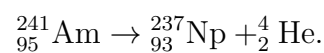
The specific activity is the activity per unit mass of the radionuclide. There are various decay processes, the most important of which are presented in the following.

2.1.1. α -decay

The α decay describes the emission of a Helium nucleus ${}^4_2\text{He}$ (α -particle) [3, pp. 6-7]:

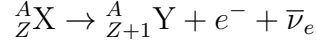


${}^{241}_{95}\text{Am}$ is an example of an α emitting radionuclide:

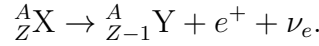


2.1.2. β -decay

In a β -decay, an electron and an electron antineutrino are emitted due to the conversion of a neutron into a proton (β^- -decay, [3, pp. 3-5]) or a positron and an electron neutrino are emitted due to the conversion of a proton into a neutron (β^+ -decay, [4, p. 29])⁽¹⁾. In case of a β^- -decay this is written as:



while for a β^+ -decay this reads:

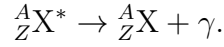


${}^{60}\text{Co}$ is an example of a β^- -decay:



2.1.3. γ Emission

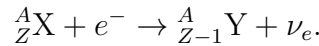
Excited nuclei, for example produced by a β -decay, may lose their excess energy by emission of a high energy photon (gamma) [3, pp. 11-12]:



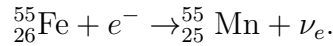
When ${}^{60}\text{Co}$ decays by the β decay, it leaves the produced ${}^{60}\text{Ni}$ nucleus in an excited state, which almost instantaneously de-excites by emission of two γ with energies of 1.17 MeV and 1.33 MeV respectively.

2.1.4. Electron Capture

An unstable nucleus may be able to capture one of its orbital electrons and convert a proton into a neutron by emission of an electron neutrino [4, pp. 33-35]:



The vacancy of the captured electron is filled by electrons from higher energetic levels, resulting in the emission of X-rays or so-called Auger electrons. ${}^{55}\text{Fe}$ is an example for such a process:



⁽¹⁾Since the mass of the neutron is larger than the one of the proton, the protons and neutrons in the nucleus need to rearrange and become more tightly bound to enable this decay [4, p. 29].

2.2. Interaction of Radiation with Matter

When particles pass through matter, they can undergo different types of interactions with the matter. The probability of interactions depends on the particle's characteristics such as particle type, energy, mass and charge and on the matter characteristics such as density and atomic number of its atoms. The so-called cross section σ is a measure for this probability [5, p. 23] and is defined by:

$$\sigma = \frac{\text{reaction rate}}{\text{flux of particles} \cdot \text{number of scattering centres}}. \quad (2.3)$$

With the luminosity $\mathcal{L}$ this can be rewritten to:

$$N = \sigma \mathcal{L} \quad (2.4)$$

where N is the number of reactions per unit time. In the case of a fixed target experiment, where a beam of intensity $I = N_{\text{beam}}/\text{time}$ hits a target with density ρ , thickness d and a number of target nuclei per unit volume $n = \rho \frac{N_A}{M_{\text{mol}}}$, the luminosity is given by [2, p. 23-24]:

$$\mathcal{L} = I \cdot n \cdot d. \quad (2.5)$$

In particle physics, the unit of the cross section is the barn with $1 \text{ b} = 10^{-28} \text{ m}^2$. The most important interactions for this work are presented in the following.

2.2.1. Heavy Charged Particles

Any charged particle heavier than an electron is called a heavy charged particle. Therefore carbon ions and protons used for measurements at the Italian National Centre of Oncological Hadrontherapy (CNAO) both fall into this category and the focus in this section is put on the processes needed to understand the so-called Bragg curve.

Stopping Power

The total energy loss of heavy charged particles is caused by many interactions mainly with the electrons of the matter the particles slow down in. Each interaction transfers on average only a small amount of energy caused dominantly by ionisation of atoms. If the produced secondary electron has enough energy to ionise atoms itself, it is called a δ -ray. The Bethe formula [6, p. 442] describes the mean rate of energy

loss for particles between $0.1 \lesssim \beta\gamma \lesssim 1000$ (for protons: $5 \text{ MeV} \lesssim E_{kin} \lesssim 1 \text{ TeV}$; for carbon ions: $5 \text{ MeV/u} \lesssim E_{kin} \lesssim 1 \text{ TeV/u}$):

$$\langle -\frac{dE}{dx} \rangle = K z^2 \frac{Z}{A} \frac{1}{\beta^2} \left[\frac{1}{2} \ln \frac{2m_e c^2 \beta^2 \gamma^2 T_{\max}}{I^2} - \beta^2 - \frac{\delta(\beta\gamma)}{2} \right]. \quad (2.6)$$

Table 2.1 explains the variables used in equation 2.6. The quantity $-dE/dx$ is often referred to as stopping power. The most probable energy loss is much smaller than the average energy loss calculated by the Bethe formula since the average is dominated by very rare interactions with a large energy transfer [6, p. 442].

Table 2.1.: Explanation of symbols used in equation 2.6

Symbol	Definition	Value (if constant)
E	energy of particle	
x	path unit	
β	ratio of particle speed to light speed (v/c)	
γ	Lorentz factor	
K	$4\pi N_A r_e^2 m_e c^2$	$0.307\,075 \text{ MeV mol}^{-1} \text{ cm}^2$
N_A	Avogadro's number	$6.022 \times 10^{23} \text{ mol}^{-1}$
r_e	classical electron radius	2.818 fm
$m_e c^2$	electron mass $\times c^2$	511 keV
z	charge number of incident particle	
Z	atomic number of absorber	
A	atomic mass of absorber	
$T_{\max}$	maximum energy transfer in one collision	
I	mean excitation energy	
$\delta(\beta\gamma)$	density effect correction	

The validity of the Bethe formula can be extended to lower energies down to $\beta \approx 0.05$ (protons: $E_{kin} \approx 1 \text{ MeV}$) by taking into account several corrections [6, p. 444]. For even smaller energies there are other models to describe the energy loss: the phenomenological fitting formulae by Andersen and Ziegler are usually used for protons for $0.01 \lesssim \beta \lesssim 0.05$ (protons: $50 \text{ keV} \lesssim E_{kin} \lesssim 1 \text{ MeV}$; [6, p. 444], [7]). Below $\beta \lesssim 0.01$ (protons: $E_{kin} \lesssim 50 \text{ keV}$), a theoretical description applies which was first outlined by Lindhard and Scharff [8].

Figure 2.1 shows the stopping power of protons and carbon ions in water.

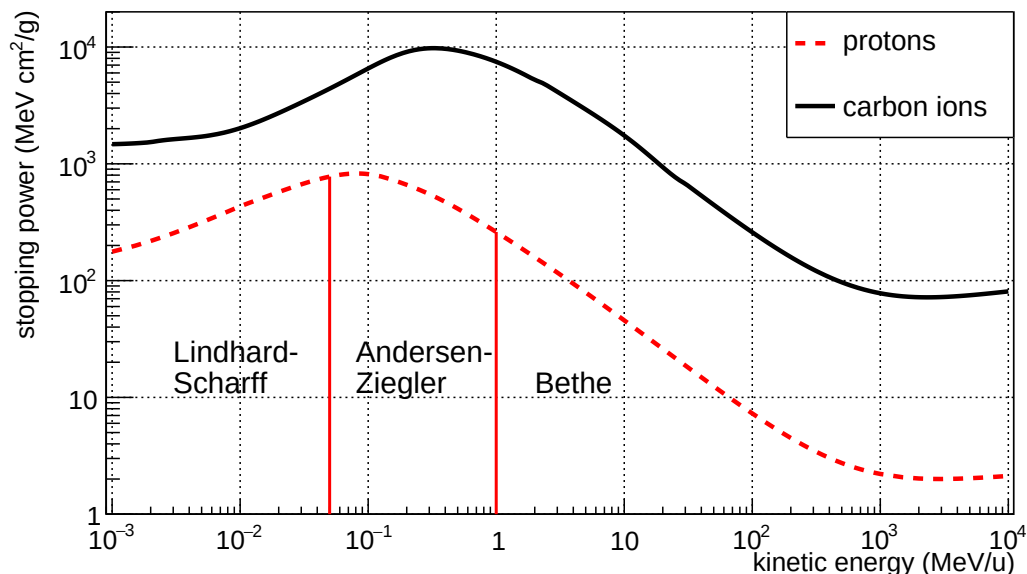


Figure 2.1: Total stopping power of protons (dashed red line) and carbon ions (black line) in water. Graph produced using the online database pstar of the United States National Institute of Standards and Technology (NIST) [9] and the software SRIM [10] for protons and carbon ions respectively. Vertical lines show approximate limits between stated models.

Nuclear Reactions

For this work the most important nuclear reactions are (in)elastic scattering and fragmentation. If there are the same particles in the initial and in the final state, scattering occurred. Elastic scattering describes a process in which the direction of the incoming particle is changed but the sum of the kinetic energies of the particles is conserved. The reaction is called inelastic scattering when energy is transferred so that a particle is excited. The main effect of elastic Coulomb interactions with the target nuclei is the lateral spread out of the beam. Figure 2.2 shows the calculated beam spread for protons and carbon ions of several different energies.

A carbon ion is a composed nucleus and can therefore undergo nuclear fragmentation with an important contribution to the total deposited dose of the projectile fragments. Figure 2.3 shows a sketch of a possible description: a projectile nucleus hits a target nucleus and both get disintegrated with the formation of many fragments. As the projectile fragments are lighter than the initial projectile nucleus but their kinetic energy is large, the range of the fragments is larger, which leads to the so-called fragmentation tail of the Bragg curve. The angular distribution of the

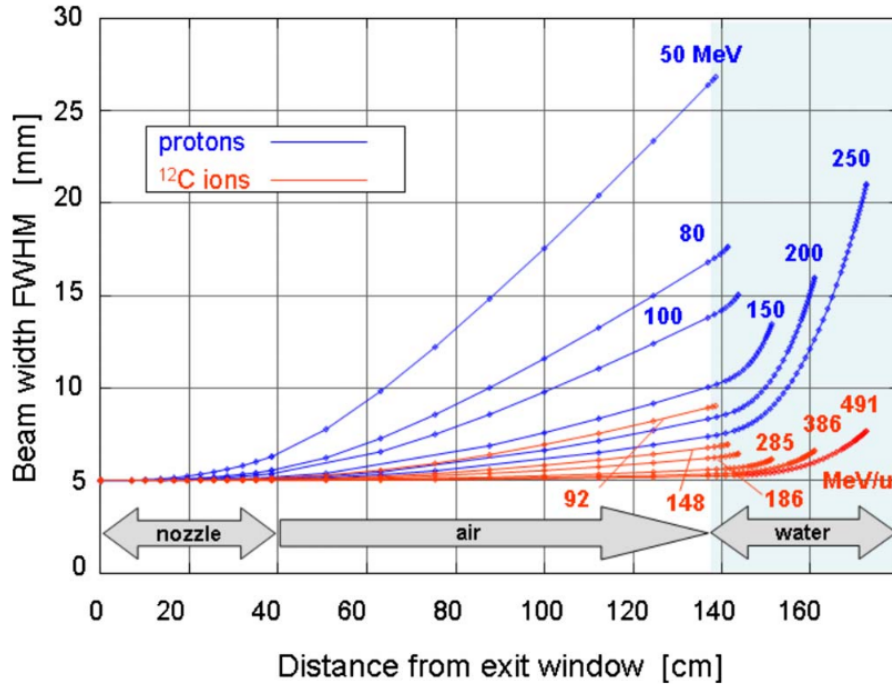


Figure 2.2: Calculated beam spread out in a typical treatment line with a nozzle, a path in air and a patient (water), when an initially parallel beam with FWHM 5 mm is assumed. Figure by U. Weber, Rhön-Klinikum AG, published in [11].

fragments is strongly boosted in beam direction but nevertheless larger than the initial beam spread and therefore contributing to the spread out of the beam.

Although only carbon ions can produce fragments contributing to the fragmentation tail, nuclear reactions are also important for protons: a non-negligible fraction of beam particles is lost due to inelastic nuclear interactions, reducing the fluence of the beam while passing through matter [13]. For example the fluence reduction of a proton beam in water is approximately 20% in the last 20 cm of range [14].

The Bragg Curve

The Bragg curve describes the energy deposition of hadrons in dependence of their penetration depth and is named after William Henry Bragg who discovered around 1900 that the 'alpha-particle is a more efficient ioniser towards the extreme end of its course' [15]. From the Bethe formula (equation 2.6) a sharp Bragg curve would be expected, because a specific energy loss is associated with a particle energy. However, the Bethe formula only represents an average value and the energy loss

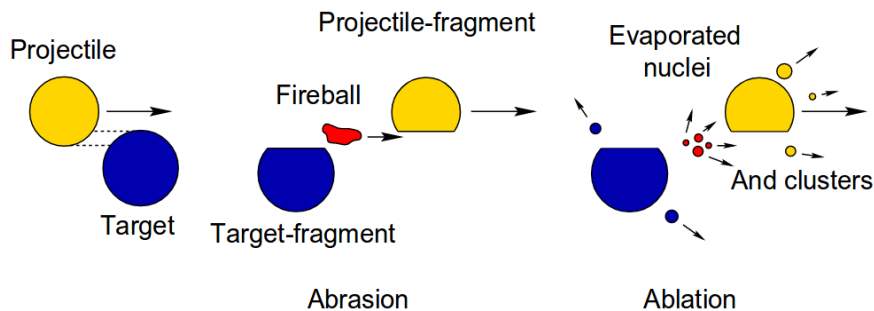


Figure 2.3: A nuclear reaction of a projectile and target nucleus can be described in an abrasion-ablation model with the intermediate formation of a fireball. Figure from [12].

and therefore the range of a single particle is also determined by the statistical nature of the interactions. The fluctuation of the range is called range straggling and results in a broadened Bragg peak. Nuclear interactions add a fragmentation tail for carbon ions. Figure 2.4 shows measured and simulated Bragg curves for protons and carbon ions at CNAO, covering the typically used energies / ranges. Figure 2.5 shows the contribution of secondary particles to a Bragg curve of carbon ions.

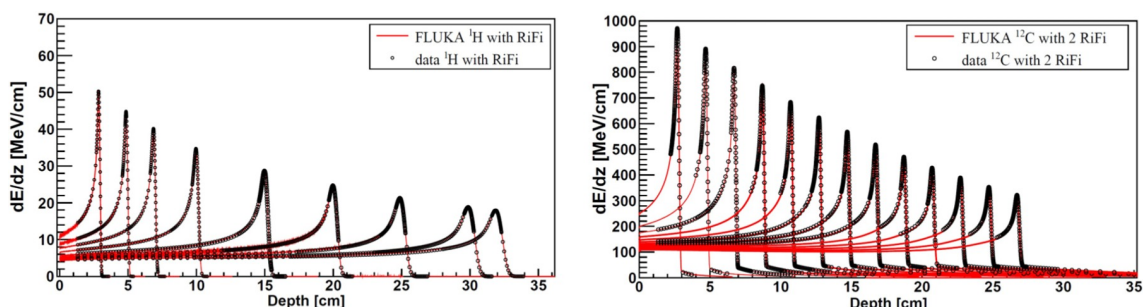


Figure 2.4: Measured and simulated Bragg curves for protons (left) and carbon ions (right) at CNAO for typical ranges for cancer treatment [16].

2.2.2. Electrons

Electrons undergo collisional and radiation energy losses. The total energy loss is the sum of the two:

$$\left(\frac{dE}{dx}\right)_{\text{total}} = \left(\frac{dE}{dx}\right)_{\text{coll.}} + \left(\frac{dE}{dx}\right)_{\text{rad.}}. \quad (2.7)$$

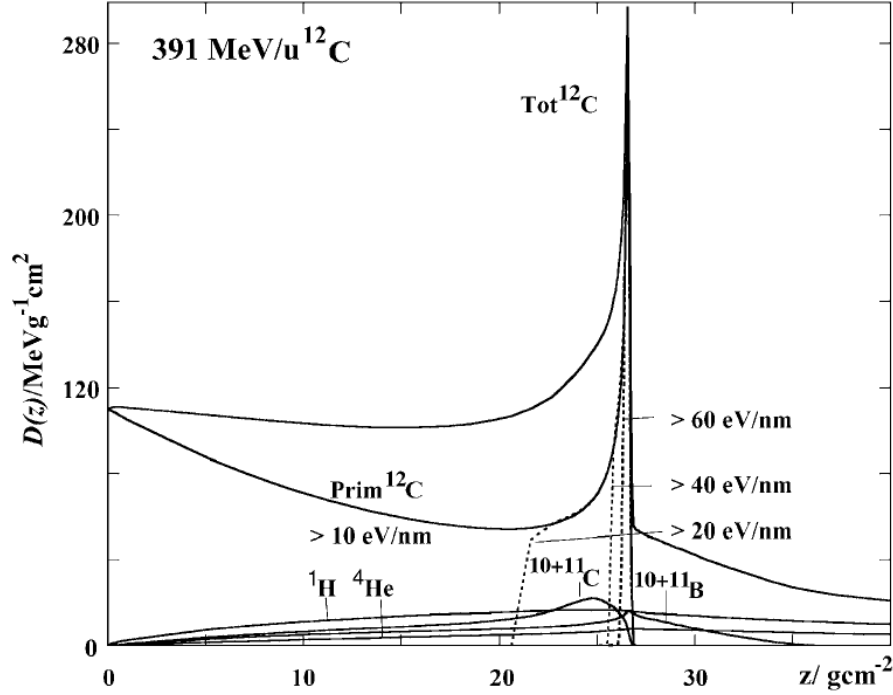


Figure 2.5: The dose deposited by secondary particles is important for the whole Bragg curve of carbon ions, especially for the fragmentation tail [17]. Major contributions are from protons, Helium, ^{10}B and ^{11}B and ^{10}C and ^{11}C .

The collisional energy loss of electrons cannot be calculated with the Bethe equation (equation 2.6) as they collide also with electrons and therefore the collision partners are of the same mass and kind. The assumption needed for the Bethe formula that the incident particle does not change its direction does not hold in this case and the particles are also indistinguishable. The formula for the energy loss of electrons is ([18, p. 37-38], rewritten in the notation explained in table 2.1 and with the same corrections as in equation 2.6):

$$-\left(\frac{dE}{dx}\right)_{\text{coll.}} = \frac{1}{2} K \frac{Z}{A} \frac{1}{\beta^2} \rho \left[\ln \frac{E^2 (E+2)}{2 (I/m_e c^2)^2} + (1 - \beta^2) + \frac{\frac{E^2}{8} - (2r_e + 1) \ln 2}{(E+1)^2} - \delta(\beta\gamma) \right]. \quad (2.8)$$

At higher energies the energy loss due to radiation dominates. According to classical theory any charged particle must radiate when accelerated and deflection of electrons in matter is such an acceleration [3, p. 44]. The radiation is due to Bremsstrahlung or electromagnetic radiation and the energy loss is calculated by [3, p. 44]:

$$-\left(\frac{dE}{dx}\right)_{\text{rad.}} = \frac{NEZ(Z+1)e^4}{137m_e^2c^4} \left(4\ln\frac{2E}{m_e c^2} - \frac{4}{3}\right). \quad (2.9)$$

The notation is the same as explained in table 2.1. Since this energy loss is proportional to $Z(Z+1)$ and $E \cdot \ln(E)$, it dominates at higher electron energies and in materials with large atomic number. Figure 2.6 shows the different contributions in dependence of the electron energy.

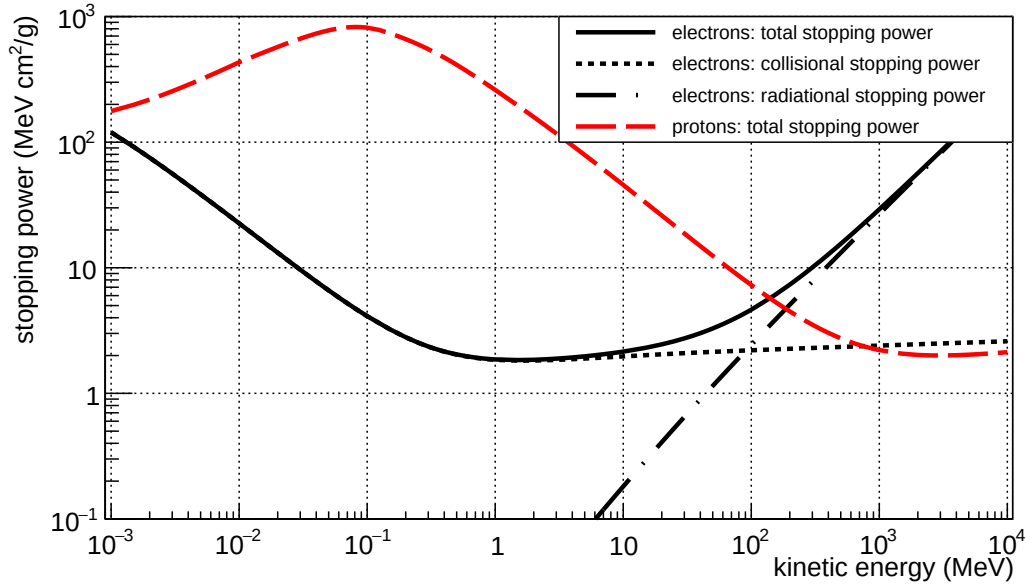


Figure 2.6: Total, radiative and collisional stopping power (black lines) of electrons and total stopping power of protons in water (red line). Graph produced using the online databases *estar* and *pstar* of the NIST [9] for electrons and protons respectively.

2.2.3. Photons

Photons interact via three main processes: photoelectric effect, scattering and pair production. The intensity I of a photon beam decreases exponentially with the distance x travelled in a material of attenuation coefficient μ [18, p. 53]:

$$I(x) = I_0 \exp(-\mu x). \quad (2.10)$$

Photoelectric Effect

At small photon energies the absorption of the photon and subsequent ejection of an electron is the dominant process. In this photoelectric effect the energy of the electron is [18, p. 54]:

$$E_e = E_\gamma - E_{\text{binding}} \quad (2.11)$$

where E_e is the energy of the outgoing electron, E_γ is the energy of the incident photon and E_{binding} the binding energy of the atom electron.

Scattering

Photons can undergo elastic and inelastic scattering. Elastic scattering is dominated by Rayleigh scattering. The most important process of inelastic scattering is Compton scattering, which is the dominant photon interaction at intermediate energies. In this process the photon scatters off an electron, suffering changes in energy and direction. The energy E'_γ of the photon after the scattering is [3, p. 51]:

$$E'_\gamma(\theta) = \frac{E_\gamma}{1 + \frac{E_\gamma}{m_e c^2} (1 - \cos(\theta))}. \quad (2.12)$$

Here, E is the photon energy before the reaction and θ the scattering angle between the incident and the scattered photon.

Pair Production

The production of an electron-positron pair by a photon is called pair production. It can take place only above the energy threshold of two times the electron rest mass (1.02 MeV) and in the presence of an electromagnetic field, typically that of the nucleus [19, p. 146]. Figure 2.7 shows the cross sections for the main processes.

2.3. Physics of Particle Detection in Gases

Particle detectors measure one or more properties of particles, for example the number of particles, their position, their energy or their time of arrival. In order to perform the measurement, an interaction with a detection volume – which can be a gas – is required. Gaseous detectors are typically based on the ionisation of the detection gas – i.e. the production of one or more electron-ion pairs – followed by the drift of the charge towards a readout, possible multiplication and measurement in a readout.

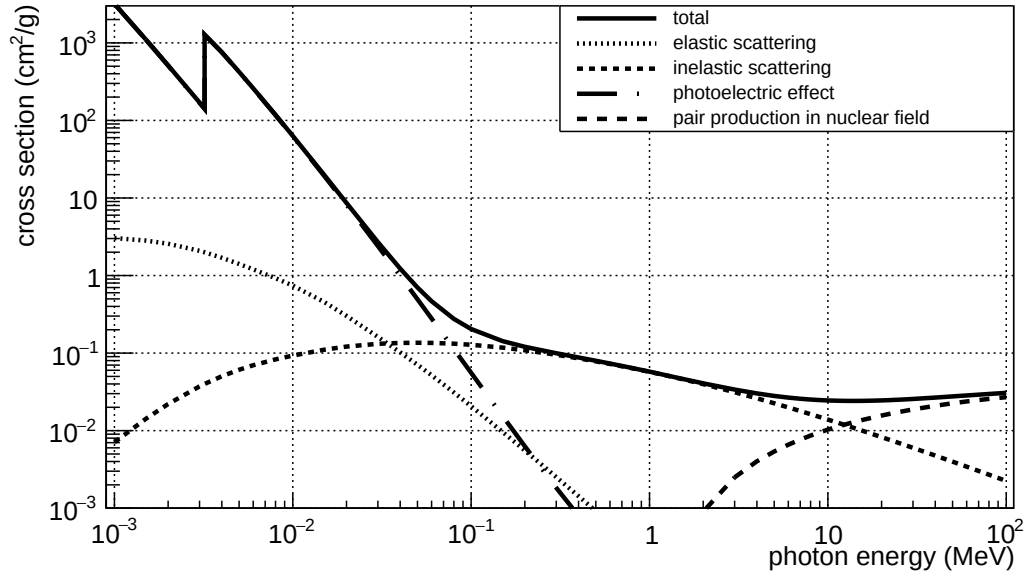
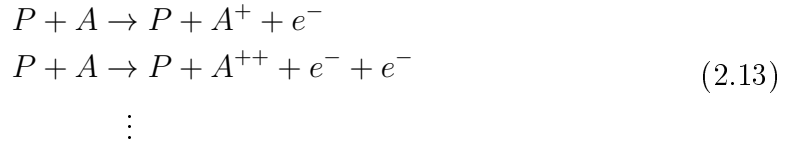


Figure 2.7: Cross section of the four dominant processes for photons in Argon. Graph produced using the online database XCOM of the NIST [20].

2.3.1. Primary Charge Creation, Drift and Diffusion

Typically a distinction is made between primary and secondary ionisation [21, pp. 3-4]. Primary ionisation refers to the direct emission of one or more electrons e^- of an atom A hit by the incoming particle P :



If one or more intermediate steps are needed, the ionisation is referred to as secondary. In case of a δ -ray, the same process as above takes place followed by the ionisation of another atom by the electron produced before. Another possibility is the excitation of an atom A^* by:



or:



followed by the de-excitation of A^* and ionisation of another atom B



In gaseous detectors A^* is often the metastable state of a noble gas atom (for the GEMPix typically Argon) and B is an atom of the so-called quencher gas (e.g. CO_2). In this case the process is called Penning effect [21, p. 4].

Depending on the particle and its energy one or more primary electrons are created and the particle will deposit a part or the total of its energy in the gas. A 5.9 keV photon of ^{55}Fe will undergo the photoelectric effect and eventually create about 150 electrons in a typical GEMPix set-up (see below for the calculation). A primary carbon ion at CNAO will create a track of ionisation, depositing only a small fraction of its energy and producing hundreds of electrons. The average energy value W to produce an electron-ion pair is typically in the range of 25 eV to 35 eV depending on the gas mixture [3, p. 130]. If a simple composition law for gas mixtures is applied, it is about 38 eV for $\text{Ar}:\text{CO}_2:\text{CF}_4$ (45:15:40) due to the exceptionally large W value of CF_4 ⁽²⁾. The number of electron-ion pairs N created is calculated by [23, p. 28]:

$$N = \frac{\Delta E}{W} \quad (2.17)$$

where ΔE is the total energy loss of the incoming particle. Therefore about 150 electrons per 5.9 keV photon are expected for $\text{Ar}:\text{CO}_2:\text{CF}_4$ (45:15:40).

Once an electron-ion pair is created, the charges need to be prevented from recombination and drifted towards the readout. This is achieved by applying an electric field, often named drift field. Electrons are accelerated by the electric field until they collide with a gas molecule and change their direction. Afterwards, the acceleration by the field takes place again, leading to an electron cloud with global motion towards the electrode, called drift, and a spread out of the cloud, called diffusion.

The drift velocity v is calculated by [3, p. 133]:

$$v = \frac{\mu E}{p} \quad (2.18)$$

where E is the electric field strength and p the gas pressure. The mobility μ depends in general on gas type, electric field and pressure. The drift velocity of ions is several orders of magnitude smaller due to the larger mass [23, p. 21]. For electrons in the GEMPix drift region it is more than 1 cm/ μs [24].

The classical diffusion formula is [23, p. 81]:

$$\sigma = \sqrt{2Dt} \quad (2.19)$$

⁽²⁾The W values for the used gases are 26 eV for Argon, 34 eV for CO_2 and 54 eV for CF_4 [6, p. 465]. In an approximate calculation [22, p. 242], these values are simply weighted by the proportion of the corresponding gas in $\text{Ar}:\text{CO}_2:\text{CF}_4$ (45:15:40).

where σ is the standard deviation of the width of the charge cloud, D is the diffusion coefficient (gas dependent) and t is the diffusion time. D can be split up into a lateral and a transversal component, following the electric field and therefore the direction of electron acceleration. Figures 2.8a and 2.8b show the drift velocity and diffusion respectively for Ar:CO₂:CF₄ (45:15:40).

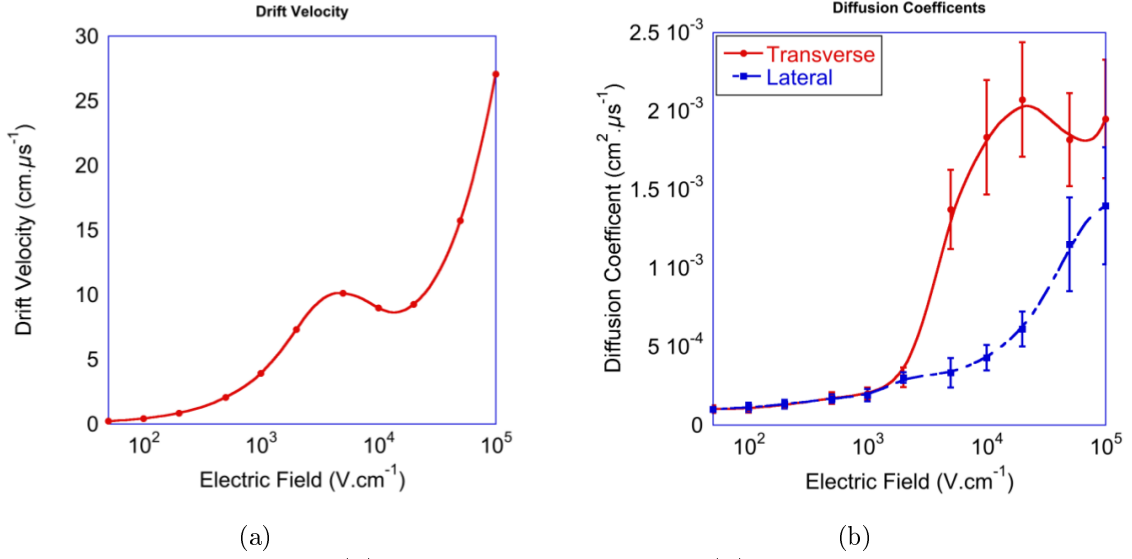


Figure 2.8: Drift velocity (a) and diffusion coefficient (b) for electrons in Ar:CO₂:CF₄ (45:15:40). Calculated by Filippo Resnati (CERN) using Magboltz ([25], [26]), graphs first published in [27, p. 123].

2.3.2. Avalanche Multiplication

An electron produces another electron after an average distance (or mean free path) λ , where the inverse $\alpha = \lambda^{-1}$ is called the first Townsend coefficient. The relation of α to the ionisation cross section σ_i is [23, p. 144]:

$$\alpha = n\sigma_i \quad (2.20)$$

where n is the number of molecules per unit volume. The number of new electrons dN produced by N_0 electrons in a distance dx is then [28, p. 57]:

$$dN = \alpha N_0 dx. \quad (2.21)$$

Assuming that α is constant over the travelled path – i.e. that the electric field does not depend on the position – equation 2.21 can be integrated to yield the total number of electrons after multiplication N :

$$N = N_0 \exp(\alpha x). \quad (2.22)$$

The ratio N/N_0 is defined as the multiplication factor or gain G :

$$G = \frac{N}{N_0} = \exp(\alpha x). \quad (2.23)$$

The Townsend coefficient depends on many parameters, the most important ones being the type of gas, the density of gas atoms (i.e. the pressure and temperature in the detection gas) and the applied electric field ([29], [30]). It is zero for small electric fields because the electron must overcome a threshold energy before multiplication takes place. Above this threshold α increases strongly with the electric field. Many parametrisations for the Townsend coefficient exist (see e.g. [30]), a common one is [28, p. 57]:

$$\frac{\alpha}{p} = A \exp\left(-\frac{Bp}{E}\right) \quad (2.24)$$

where p is the gas pressure, A and B are constants depending on the gas (mixture) and E is the electric field⁽³⁾. Figure 2.9 shows the Townsend coefficient for Ar:CO₂:CF₄ (45:15:40) in dependence of the electric field.

Usually a linear dependence between α and E (as proposed in [31, p. 71]) is assumed for GEMs and therefore the gain depends on the applied GEM voltage $V \propto E$ by:

$$G \propto \exp(V). \quad (2.25)$$

It is clear that this assumption is only valid in a very limited regime of the electric field, as can be seen in figure 2.9. In the case of a triple GEM detector equation 2.25 transforms to:

$$G \propto \exp(V_1) \cdot \exp(V_2) \cdot \exp(V_3) \quad (2.26)$$

$$\Rightarrow G \propto \exp(V_1 + V_2 + V_3) \quad (2.27)$$

In the GEM literature it is quite common to refer to the voltage as the gain since this is typically the only dependence (e.g. ‘a gain of 1240 V was applied’).

⁽³⁾More generally, the denominator p in equation 2.24 is replaced by the gas density N at a certain pressure and temperature [30].

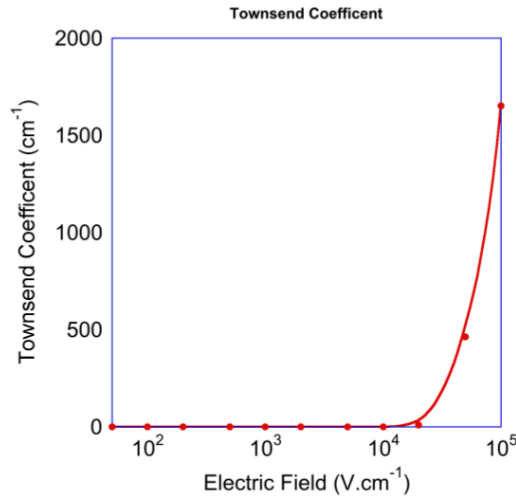


Figure 2.9: Townsend coefficient for electrons in Ar:CO₂:CF₄ (45:15:40). Calculated by Filippo Resnati (CERN) using Magboltz [25],[26], graph first published in [27, p. 123].

2.4. Software

The main software packages that were used for data acquisition, data analysis and simulation are briefly introduced in this section.

2.4.1. Pixelman

Pixelman [32] is a data acquisition and processing software package for Timepix, Medpix2 and Medpix3 using the FITPix readout [33]. It was developed by a group at the Institute of Experimental and Applied Physics of the Czech Technical University in Prague and offers a Graphical User Interface (GUI) from which not only settings can be changed but also data acquisition is controlled and which immediately visualises the data. Figure 2.10 shows a screenshot of the GUI. Pixelman is used for this work to set up the detector, take data and in some cases to perform the first analysis step: predefined routines such as the threshold equalisation (see section 3.2.6) are important before data can be acquired; settings are either set manually or a configuration file can be loaded; test data can be taken and visualised to check the data quality in a first step, e.g. to check the threshold level; a python interface (see section 2.4.4) allows the use of custom scripts to automate data acquisition, online data analysis and visualisation. In case of laboratory measurements with radioactive test sources – like for measurements with an ⁵⁵Fe source – a cluster

analysis (see section 4.3.1) is typically performed before writing data to a file, while all raw data are written to a file for measurements at CNAO.

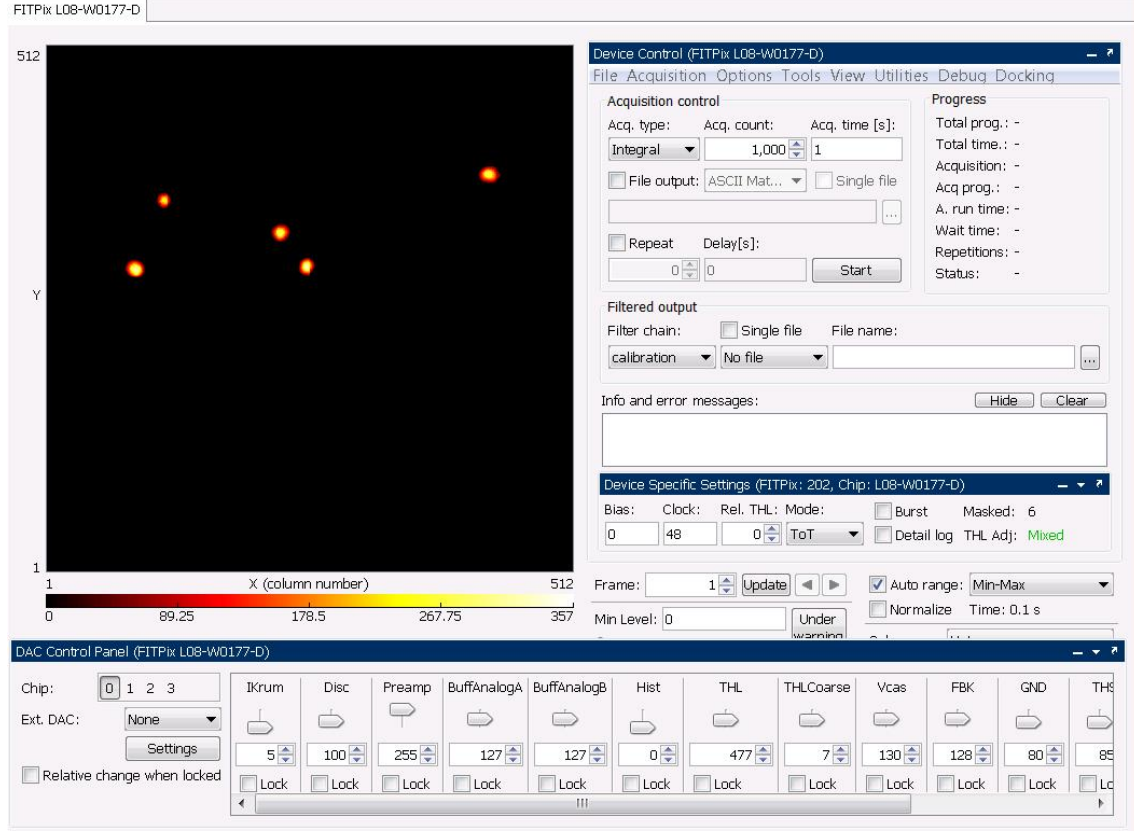


Figure 2.10: The Pixelman GUI with controls for several settings for the data acquisition (bottom and right) and a display showing an acquired frame (top left).

2.4.2. MAFalda Framework

The Medipix Analysis Framework (MAFalda) [34] is a C++/ROOT based framework for data acquired by a Medipix device. The software is available at [34] and more information can be found in reference [27]. Raw data (i.e. the counts per pixel in each frame) acquired with the GEMPix are converted into easily manageable and smaller ROOT files without loss of information. After this initial step, a custom analysis chain can be built using a set of common operations provided by the framework or custom operations. For example a cluster analysis can be carried out and the results can be visualised using the MAFalda viewer. Since the converted raw

data and data produced by the analysis are typically orders of magnitudes smaller than the raw data, MAFalda allows for fast data visualisation after data conversion. Figure 2.11 shows a screenshot of the MAFalda console.

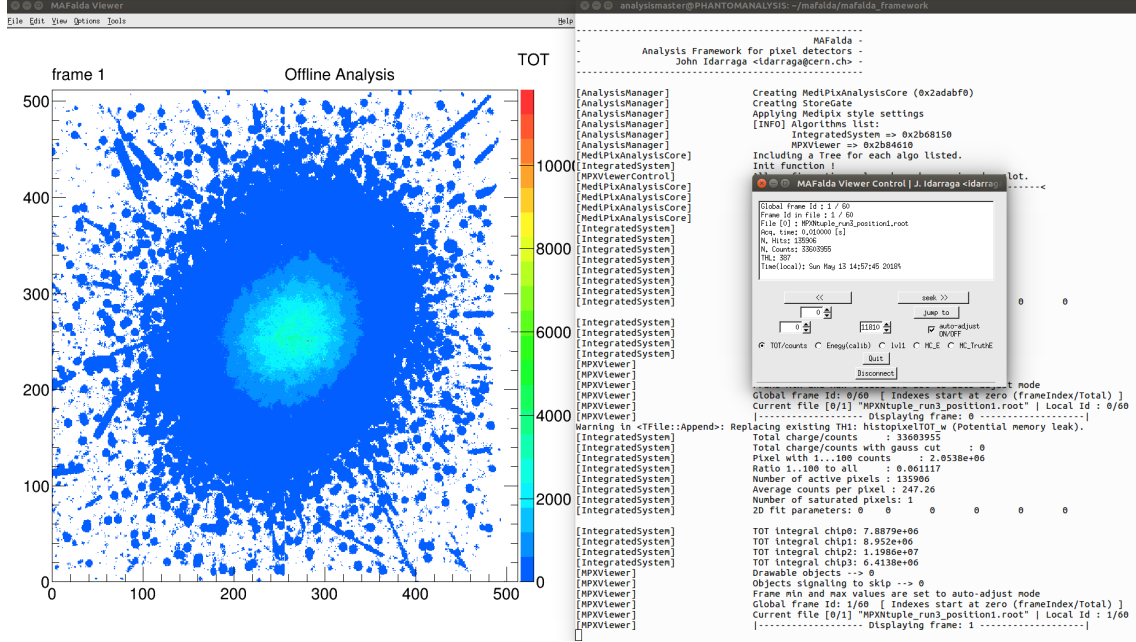


Figure 2.11: Screenshot of MAFalda viewer (left), control for the viewer (small window on the right) and terminal to start mafalda and to display customised output (right).

2.4.3. ROOT

ROOT is a data analysis framework developed at CERN [35]. Although written in C++, it can be integrated in other languages such as PYTHON. In this work it is mainly used within the MAFalda framework and for data analysis and visualisation.

2.4.4. Python

PYTHON [36] is one of the main programming languages. In this work it is used for custom scripts in Pixelman and together with ROOT for data analysis and visualisation.

2.4.5. FLUKA

Fluctuating Cascade (FLUKA) ([37], [38]) is an integrated Monte Carlo code for simulations of transport and interactions of particles. It is used in this work to simulate the beam interactions in the integrated system and generate e.g. Bragg curves for comparison to the experimental data. The history of FLUKA goes back to the 1960s when Johannes Ranft wrote the first high-energy Monte Carlo transport codes, but the present code is completely different and far more powerful [38, p. 387]. The basic principle is that for a defined problem (geometry and materials) and a certain particle source (e.g. a proton with given position and momentum vectors) a random evolution of the particle (e.g. elastic scattering) according to the underlying probability distributions (e.g. interaction cross sections) is performed. The same holds for secondary particles possibly produced. The quantities of interest such as the energy deposition in a certain volume are calculated and the process is repeated for a given number of primary particles. FLUKA is well suited for hadron therapy applications and is used for example at CNAO for the calculation of Bragg curves (see e.g. [16]). A convenient user interface for FLUKA is the FLUKA Advanced Interface (FLAIR) [39]. For this work FLUKA version 2011.2x.2 and FLAIR version 2.3-0 are used.

2.4.6. LabVIEW

The Laboratory Virtual Instrument Engineering Workbench (LabVIEW) is the environment for a visual programming language by National Instruments [40]. It is often used to control hardware, as in this work for the moving system in the water phantom and the data acquisition of the ionisation chamber. For many commercial products such as the ionisation chamber, drivers for LabVIEW are available.

3. The GEMPix Detector

The GEMPix couples two CERN technologies that are introduced in this chapter: GEMs (section 3.1) for signal amplification and Timepix (section 3.2) for readout. Results from the literature such as the radiation hardness are presented. Based on this, the GEMPix (section 3.3) is explained. Section 3.4 shows results of the detector characterisation performed in this work.

3.1. Gas Electron Multipliers (GEMs)

3.1.1. Gaseous Detectors: A Brief History

The development of the first gaseous detector, a proportional counter, can be assigned to Rutherford and Geiger in 1908 [41]. Since then several types of gaseous detectors have been developed such as the Geiger-Müller counter [42], the cloud chamber [43] and the triggered spark chamber [44]. The invention of the Multi-Wire Proportional Counter (MWPC) [45] in 1968 allowed for the first time the construction of large detectors with a high rate capability, a high spatial resolution and an electric readout. However, the spatial resolution of the MWPC is limited by the distance of the wires. To overcome this fact, micropattern gaseous detectors such as MICRO-Mesh Gaseous Structure (MICROMEGAS) [46] (1996) and GEMs [47] (1997) were developed making use of fabrication techniques of the microelectronics industries. GEMs were developed by Fabio Sauli at CERN and have found several applications thanks to their good performance and relatively easy handling.

3.1.2. Introduction to Gas Electron Multipliers (GEMs)

A GEM foil, from now on simply called GEM, consists of a thin Kapton layer serving as an electric insulator with copper layers on both sides. Holes are etched into the foil and a high voltage is applied between the two copper layers. Figure 3.1 shows a microscopy image of a GEM. The standard GEM used for the GEMPix has 70 μm holes, 140 μm hole pitch and a thickness of 50 μm [23, p. 384]. Due to the thin

Kapton layer, very large electric fields and therefore gains can be reached. Electric field strengths E of up to 100 kV/cm are possible, as motivated by:

$$E = \frac{U}{d} = \frac{500 \text{ V}}{50 \text{ } \mu\text{m}} = 100 \text{ kV/cm} \quad (3.1)$$

when using typical values for the maximum applied voltage U and the distance d between the electrodes (in this case the two copper layers of a GEM).

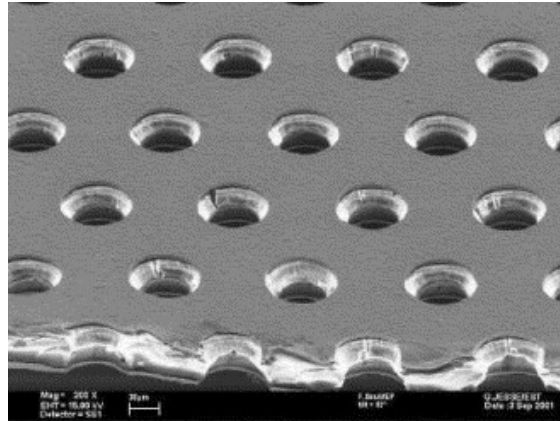


Figure 3.1: Electron microscopy image of a GEM [48]. The holes' diameter and pitch are 70 and 140 μm respectively and the thickness of the GEM is about 50 μm .

The region with a large electric field and therefore the amplification region is well confined and any charge produced by ionisation travels the same distance in this region, yielding a constant gain. Figure 3.2 shows the electric field close to a GEM hole. For stable operation of the GEM, it is better to apply a voltage smaller than the maximum possible (see section 3.1.4 for discharge and saturation phenomena). In order to achieve still larger gains, more than one GEM can be used. Each one then multiplies the number of arriving electrons and the total gain is the multiplication of the gains of each GEM (see equation 2.26). Typically achievable gains increase by one order of magnitude from single to double and from double to triple GEM detectors. Figure 3.3 shows typically achievable gains in single, double and triple GEM configurations. The exact values depend for example on the detector geometry and gas mixture. Discharge probabilities also shown in this figure are explained in section 3.1.4.

3.1.3. Detection Gas

The choice of detection gas is one of the major parameters for the performance of a gaseous detector. It affects all basic properties of the gas detection and ampli-

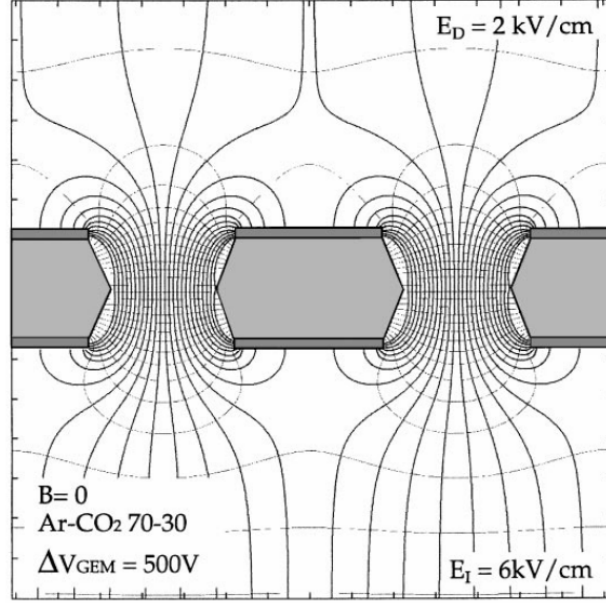


Figure 3.2: Electric field close to a GEM hole, operation conditions as stated in the image [49]. The field is the strongest inside the GEM hole, where electron multiplication takes place.

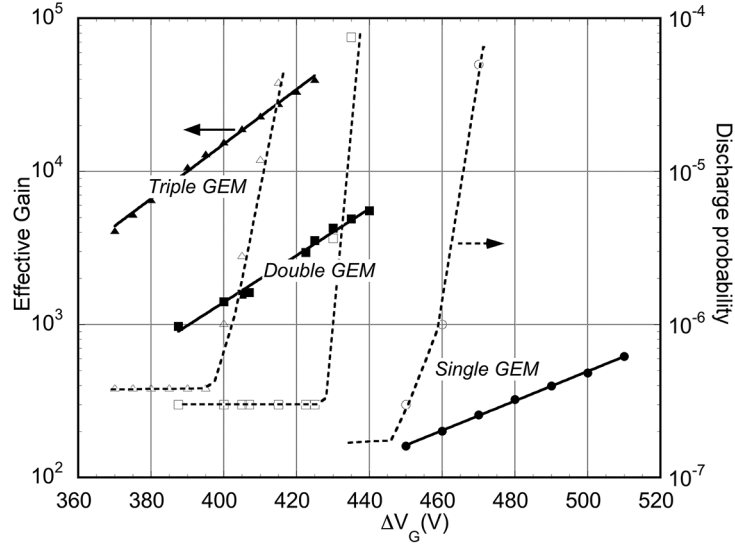


Figure 3.3: Gain (full lines) and discharge probabilities (dashed lines) for single, double and triple GEM configuration ([50], [23, p. 388]). The voltage on the x-axis is the voltage per GEM, i.e. at 400 V in the triple GEM configuration the sum of the voltages is 1200 V.

cation process: the average energy for the creation of an electron-ion pair and thus the total number of electrons in the detection volume, the drift velocity, the diffusion coefficient, the Townsend coefficient and therefore the gain and the discharge probability. Figure 3.4 shows the gain of a triple GEM for different gas mixtures. In this work Ar:CO₂:CF₄ (45:15:40) is used, which was developed for the Large Hadron Collider Beauty (LHCb) experiment at the LHC [51, p. 138]. It is non-flammable, allows operation at rather high voltages and provides a very good timing resolution due to the high drift velocity. The last feature is not of great importance for the applications in this work but for the operation as a mini-Time Projection Chamber (TPC) [27]. Another choice of gas mixture could be considered (see section 5.8).

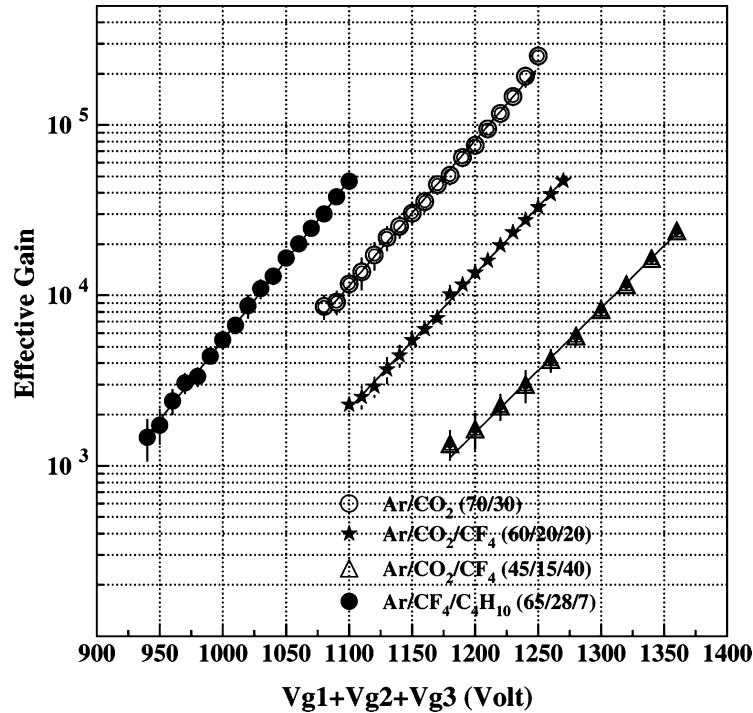


Figure 3.4: GEM gain for different gas mixtures [52]. The one used in this work is Ar:CO₂:CF₄ (45:15:40).

3.1.4. Discharges and Saturation

Discharges can be provoked by detector imperfections or surface depositions such as dust grains shortening the GEM. But even in a perfect detector there is the possibility of a streamer and eventually discharge formation. A streamer may appear when the local charge density and therefore the local modification of the electric field is large enough to lead to a cathode-directed ionisation wave [53]. Due to

the small distance between electrodes, the streamer is likely to establish a highly conducting channel between the electrodes and breakdown takes place [50]. The classical maximum number of electrons N above which an avalanche very likely turns into a breakdown is called Raether limit and is defined as [54, p. 131]:

$$N = GN_0 \approx 10^8 \text{electrons} \quad (3.2)$$

where G is the gain and N_0 the number of primary electrons. It was established that a similar limit in the order of 10^6 to 10^7 electrons also applies to GEMs at low count rates ([55], [56]).

Saturation or, more general, unwanted gain modifications in GEMs, happen in case of a high gain or a high impinging particle flux. Stable gain has been observed up to an X-ray flux of about 0.1 MHz/mm^2 [53], with the exact value depending on the gain and on the type of GEM. Above that flux, field modifications due to the high charge density lead to gain modifications. Also in case of high gains, the field modifications due to the high charge density lead to saturation. However, there is an important difference between the two scenarios: in both cases the charge density per GEM hole matters but at low particle flux the saturation must occur due to single events. This offers possibilities to establish higher gains at low flux avoiding saturation. First of all the maximum charge per GEM hole is reduced by using multiple GEMs instead of a single GEM: due to diffusion between the GEMs, the electron cloud is spread out over more GEM holes in case of a multiple GEM structure. Figure 3.3 shows the discharge probabilities for single, double and triple GEM detectors. Another possibility in a multiple GEM set-up is the asymmetric distribution of the gain over the different GEMs. The maximum charge density occurs at the last GEM, after multiplication in the other GEMs has already taken place. By lowering the voltage of the last GEM and increasing the one of the others, the charge density per hole in the last GEM is reduced. Both measures decrease the discharge probability and the saturation ([53], [50], [57]). Figure 3.5 shows the advantage of a voltage unbalance in terms of a lower discharge probability.

3.1.5. Radiation Hardness and Ageing

Ageing of gaseous detectors refers to a permanent damage and change in performance due to radiation. It is not a GEM specific issue but has been noticed for example a long time ago for MWPCs [58]. The main reason for ageing are typically deposits on electrodes due to molecular dissociation or polymerisation [23, p. 441]. Special care needs to be taken if the gas mixture contains CF_4 , as the fluorine liberated in avalanches is chemically very reactive and enlargement of the GEM holes due to etching has been observed ([59], [60], [61]). Since GEMs are comparably

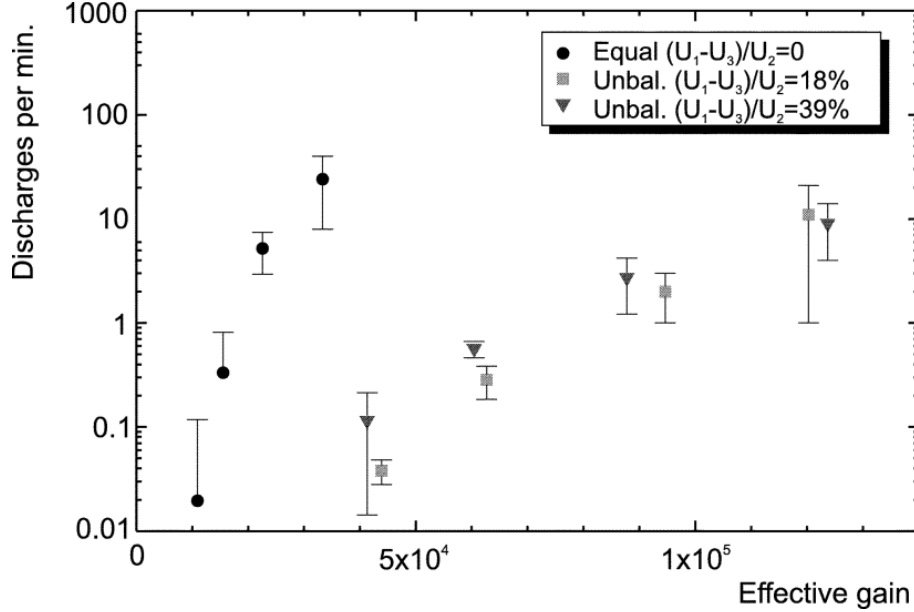


Figure 3.5: Discharge rate for a triple GEM detector in dependence of the applied voltage unbalance between the three GEMs [57]. The sum of the voltages, i.e. the total gain, is constant.

radiation hard, they were chosen for example for the central and therefore most irradiated region of the Muon system of the LHCb detector [51, p. 137]. Figure 3.6 shows that GEMs in Ar:CO₂:CF₄ (45:15:40) can withstand at least 4 C/cm² without performance deterioration.

Under several assumptions (gain = 100; energy deposition of 220 keV per primary carbon ion in the Bragg peak, leading to about 5800 electrons; 2 · 10⁸ carbon ions per second and cm²; 50% of total time with spill) the naively expected minimum lifetime t of the GEMs at CNAO is:

$$t = \frac{4 \text{ C/cm}^2}{\text{no. of electrons on GEM/s/cm}^2} \quad (3.3)$$

$$= \frac{4 \text{ C/cm}^2}{(\text{gain}) \cdot (\text{charge of electrons/carbon ion}) \cdot (\text{no. of carbon ions/s/cm}^2)} \quad (3.4)$$

$$= \frac{4 \text{ C/cm}^2}{(100) \cdot (5800 \cdot 1.6 \cdot 10^{-19}) \cdot (0.5 \cdot 2 \cdot 10^8) \cdot 1 \text{ C/s/cm}^2} \quad (3.5)$$

$$\approx 4.3 \times 10^5 \text{ s} \approx 120 \text{ h.} \quad (3.6)$$

This number represents a lower limit since the ageing test in [52] was simply stopped after the stated irradiation. It means that the GEMs could at least withstand 120 h at highest carbon ion beam intensity in the Bragg peak at CNAO. Furthermore,

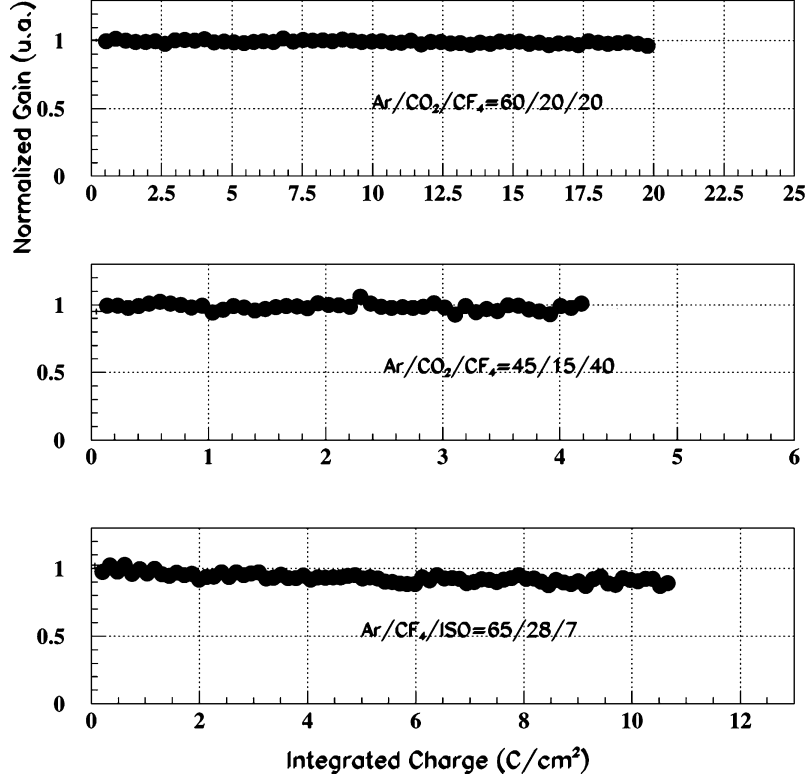


Figure 3.6: Tests of the radiation hardness of GEMs [52]. The gas mixture used in this work is Ar:CO₂:CF₄ (45:15:40).

ageing can be reduced by flushing the GEMs well with gas [61] and gain changes can be compensated by adjusting the applied gain voltage. Therefore, radiation hardness of the GEMs is regarded as sufficient for this application.

3.1.6. Charge up and Electron Transparency

An increase in the gain after turning the high voltage on and starting irradiation has been observed shortly after the invention of GEMs [62]. The effect is due to the charging up of the Kapton foil and resulting modifications of the electric field. After a certain time an equilibrium with stable gain is reached. The time depends on many parameters such as the foil geometry, the irradiation level and the water content in the gas and has been studied extensively (see for example measurements in [48], [63], [64] and simulations in [65], [66]). Typical times until the plateau gain is reached range from some minutes to several hours, with accelerated charge up in case of irradiation. In this work measurements were in general only started some hours after turning the high voltage (HV) on, therefore having reached stable gain.

Even after charge up, not all electrons that are produced in the drift region will arrive at the readout. A fraction of the electrons is lost at the GEM electrodes. The ratio of transferred electrons to originally produced electrons is called transparency and depends on parameters such as the applied electric fields and the foil geometry [59]. Transparency values close to one can be reached, decreasing significantly for example for larger drift fields and affecting the single photon detection efficiency [49]. Figure 3.7 shows the dependence on the electric fields.

3.1.7. GEM Application Overview

As GEMs can be manufactured in various sizes and shapes, have a good spatial resolution, are radiation hard and withstand high particle fluxes, they have found several applications for example in high energy physics experiments such as HERA-B [67], Common Muon and Proton Apparatus for Structure and Spectroscopy (COMPASS) ([57]), LHCb [51, pp. 137-141] and Compact Muon Solenoid (CMS) [68]. Detection of soft X-rays for radiography [69] and radiation and beam imaging using optical readout [70] are only two examples of other applications. A relatively recent overview on GEMs can be found in [59].

3.2. Timepix

3.2.1. Overview of Medipix and Timepix Chips

The Timepix chip [71] is a successor of the Medipix2 chip by the Medipix2 Collaboration [72]. It is therefore part of the Medipix chip family; its development was driven by the need for measuring the time of arrival at a possible TPC for the International Linear Collider (ILC). An overview of the Medipix and Timepix ASIC family can be found in reference [73]. The first Medipix chip, the Medipix1 was developed in the 1990s and demonstrated the noise-free counting of single photons. Originally driven by the wish to improve high energy particle physics detectors, the Medipix chips have found applications in various fields outside high energy particle physics (see section 3.2.9). Since the 1990s the Medipix1 to Medipix4 collaborations have been founded, each working on the corresponding Medipix chip. The Timepix and Timepix3 chips are based on the Medipix2 and Medipix3 chips respectively with slight modifications: the Timepix chip has for example two added readout modes compared to the Medipix2 chip.

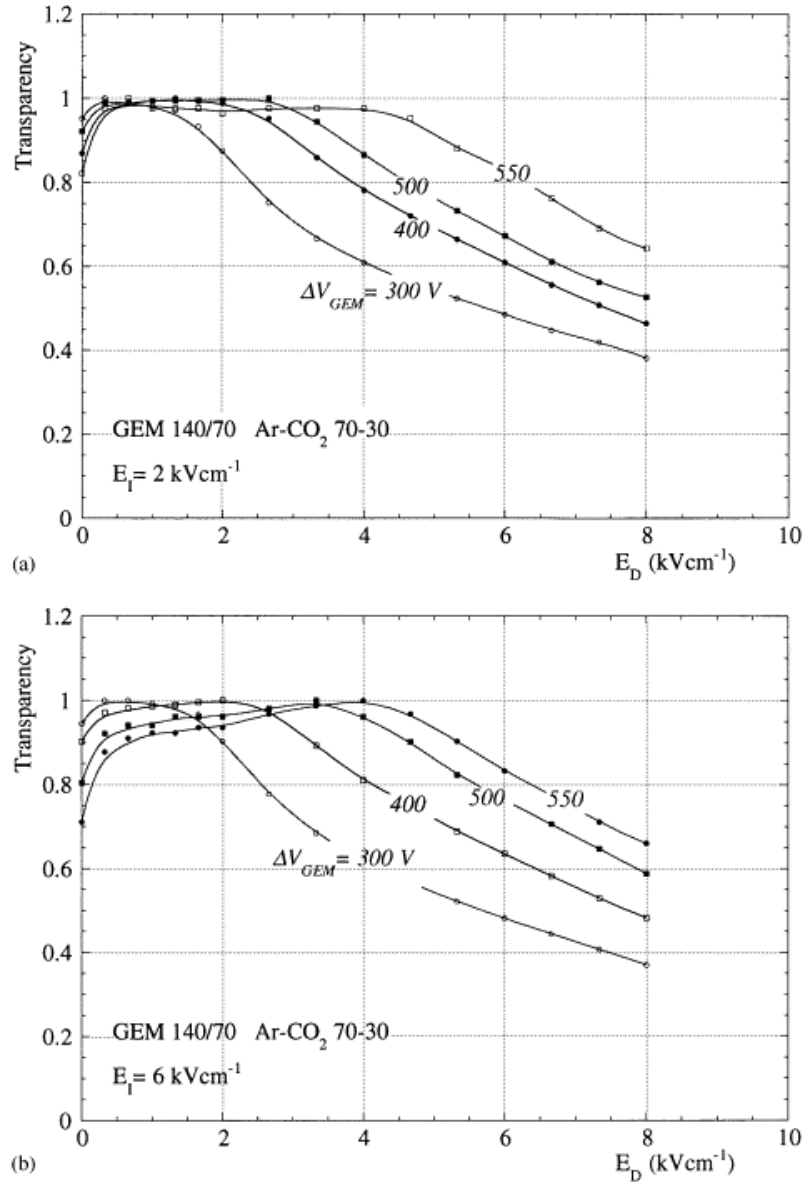


Figure 3.7: The electron transparency depends on all electric fields (drift, induction, GEM) as shown here for a standard GEM in Ar:CO₂ for low induction field (a) and high induction field (b) [49] in dependence of GEM and drift field.

3.2.2. Introduction to the Timepix

The Timepix chip is a 256×256 pixel ASIC, using $0.25\,\mu\text{m}$ complementary metal-oxide-semiconductor (CMOS) technology. Its salient features are the small pixel size of $55 \times 55\,\mu\text{m}^2$, the low noise – allowing a minimum threshold for noise-free operation of about 700 electrons – and therefore the single-photon counting capability. With its 65,536 pixels it covers an area of about $1.4 \times 1.4\,\text{cm}^2$. It is possible to couple some Timepix chips together to enlarge the sensitive area (four in case of the GEMPix). A Timepix ASIC is the readout that needs to be coupled to a suiting detection layer. Often this is a $300\,\mu\text{m}$ thick silicon sensor but other materials such as gas amplification structures for readout of gaseous detectors are possible. In this work the Timepix is always used coupled to GEMs, resulting in the GEMPix. The technical specifications of the Timepix ASIC can be found in the appendix (table A.1). Figure 3.8 shows a picture of four Timepix ASICs mounted for the GEMPix.

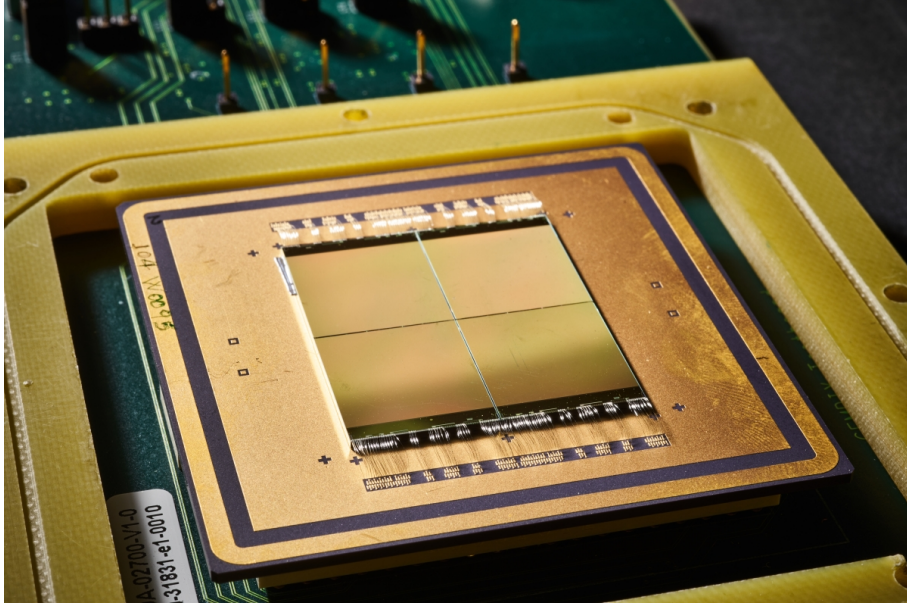


Figure 3.8: Four Timepix ASICs mounted on the ceramic board for the GEMPix (copyright: CERN).

3.2.3. Pixel Readout

The electrons arriving at each pixel produce an analogue signal that needs to be amplified and digitised, resulting eventually in a single number per pixel. Each pixel contains a pre-amplifier, a discriminator with an adjustable threshold and a 14-bit

counter (stops at 11810). The schematics of the readout can be found in the appendix (figure A.1). The pre-amplifier follows a scheme proposed by Krummenacher [74] allowing for negative and positive input signals and for pulse length adjustment by changing the input current I_{Krum} . Another important setting is the discriminator threshold: the discriminator gives out a signal if the analogue signal exceeds the set threshold. Each Timepix pixel can be masked (i.e. in case of damaged pixels) and otherwise is operated in one of the following modes:

- Medipix mode: each event is counted, i.e. if the signal exceeds the threshold the counter is incremented by one.
- Time-over-Threshold (TOT) mode: as long as the signal exceeds the threshold the counter is incremented by one at each clock tick.
- Time-of-Arrival (TOA) mode: the counter is incremented by one at each clock tick from the moment the signal exceeds the threshold until the end of the readout frame.

Figure 3.9 shows the schematics of the signal digitisation for all three readout modes. The readout of the Timepix is frame based, meaning that the acquisition is started and stopped by a trigger for all pixels synchronously irrespectively of the incoming signals. The acquisition time is adjustable and called frame length. The term frame is also used in this work to refer to the 2D count map of all pixels resulting from the acquisition during one set frame length. An externally generated and tunable clock is used as counting clock. Except for the Medipix mode, one count then translate into a time by multiplying it with the length of a clock cycle.

3.2.4. The FITPix Interface

The FITPix readout [33] is a small electronics box – approximately $6 \times 5 \times 2 \text{ cm}^3$ – providing the interface between the Personal Computer (PC) and the Timepix. Most importantly it contains a Field Programmable Gate Array (FPGA) to allow for fast and flexible control and readout of the Timepix. It does not need external power supply but is connected to a PC via Universal Serial Bus (USB) 2.0. Also, it provides the Timepix with a stable clock and can be triggered externally. The start and/or stop signal can either be an external hardware trigger – a transistor-transistor logic (TTL) signal input –, a software trigger or a timer. The following different trigger modes are available:

- software start and hardware stop
- software start and timer stop

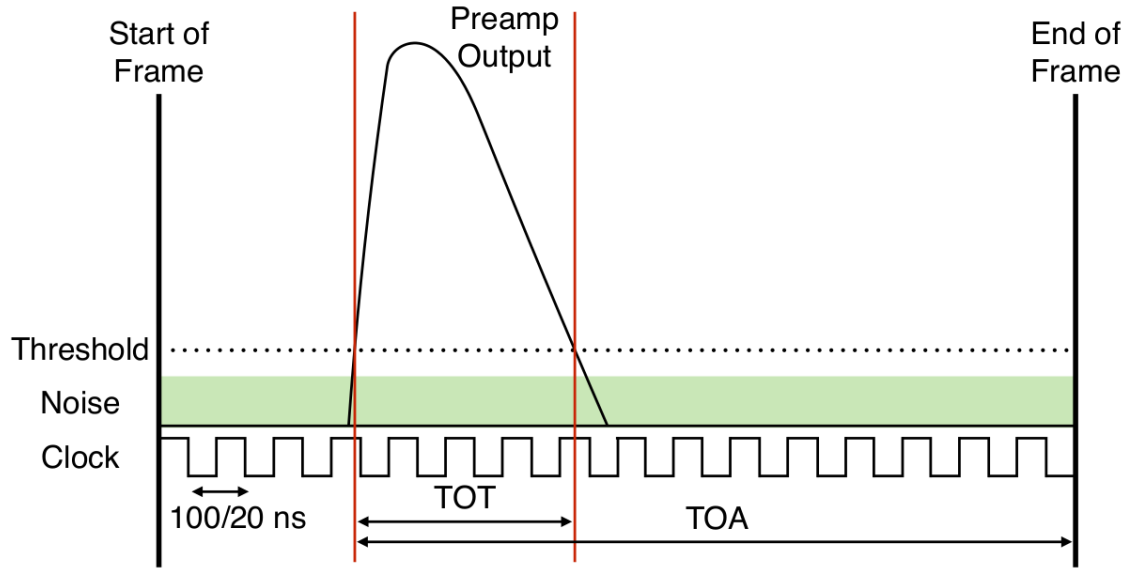


Figure 3.9: Schematic of the frame based signal discrimination in the Timepix [24]. Medipix mode would return exactly one count (because there is one event), Time-over-Threshold (TOT) mode would return the number of clock ticks between the two vertical red lines and Time-of-Arrival (TOA) mode would return the number of clock ticks between the left vertical red line and the end of the frame. The duration of a clock tick is adjustable to for example 20 ns or 100 ns.

- hardware start and timer stop
- hardware start and hardware stop.

The maximum readout speed is about 90 frames per second for a single Timepix chip connected. Up to 12 chips can be connected, while for this work four Timepix chips are connected to the FITPix interface via the GEMPix board. The accompanying software Pixelman is described in section 2.4.1.

3.2.5. Most Important Settings

The following list is non-exhaustive but provides an overview of the most important settings and how to choose these values using Timepix together with FITPix and Pixelman.

- THL: threshold for the discriminator. To be set above noise level but low enough to still properly process the signal. The threshold is defined in two

steps: a per-pixel equalisation accounts for differences in the pixels and a global threshold per chip allows for adjustment to the noise and signals.

- **IKrum:** input current for Krummenacher pre-amplifier modifying the output signal length. Higher values shorten the signal and work better for signal counting at higher rates while lower values provide better resolution for TOT mode.
- **Clock:** the acquisition clock can be set in certain steps between 2.4 MHz and 96 MHz. The shorter the clock ticks the better is the resolution for example in TOT mode. However, the number of counts increases for a faster clock and a counter overflow becomes more likely. The 96 MHz clock is rather unstable.

3.2.6. Threshold Equalisation

In the Timepix chip there is a 4-bit threshold adjustment for each pixel to compensate for slight variations in the optimal threshold value between pixels. There is a tool in Pixelman to adjust the thresholds by measuring the noise in each pixel. First of all the step size of the threshold can be adjusted by the variable THS. The step size can be optimised automatically in the Pixelman tool before starting the threshold equalisation. Two different methods to find the noise value are provided: ‘noise edge’ and ‘noise centroid’. In both cases the value of the noise is defined as counting in Medipix mode and a threshold scan is performed. As the names suggest, the ‘noise centroid’ method attempts to find the central value of the noise, which follows a Gaussian distribution, while the ‘noise edge’ method looks for the transition in and out of the noise. For measurements at low threshold the ‘noise edge’ method is therefore advantageous. In any case, a value of some threshold counts above the found noise level is usually applied by using the global threshold setting. A value of 10 to 30 counts above noise level is typical and provides a basically noise-free detector; a few pixels are usually still noisy after the equalisation and should be masked (possible in Pixelman) or discarded afterwards. Figure 3.10 shows the result of a threshold equalisation with the Pixelman tool.

3.2.7. Energy Calibration of Pixels in TOT Mode

Pixels in TOT mode measure the deposited charge and therefore the energy. The conversion from TOT counts to energy was found to follow a surrogate function $TOT(E)$ with four parameters [75]:

$$TOT(E) = aE + b - \frac{c}{E - t} \quad (3.7)$$

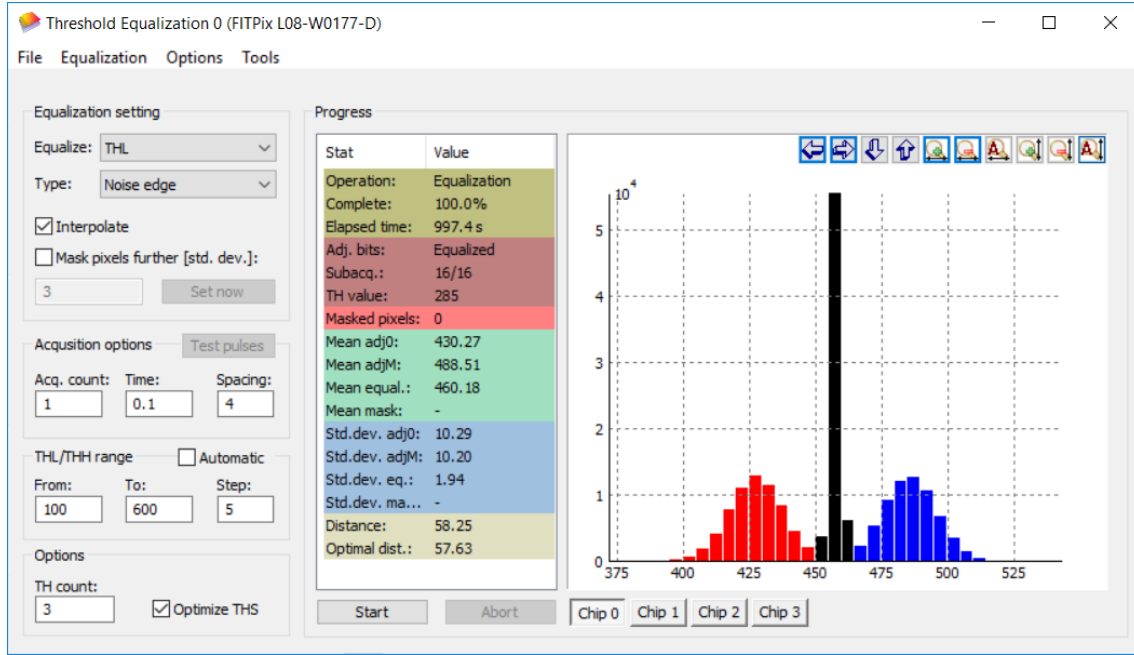


Figure 3.10: Screenshot with results of the threshold equalisation of one Timepix ASIC. On the left, there are the settings (e.g. ‘noise edge’), in the centre there are the results (e.g. the mean of the noise edge distribution) and on the right the distributions of the noise for different adjustments (in black the final equalised noise distribution).

where a , b , c and t are the four free parameters. This function can be motivated with the help of figure 3.9: if the signal was a perfect triangle and so large that the clock tick quantisation and the threshold could be neglected, the area of the signal would be proportional to the TOT counts. In reality non of these conditions holds. The applied threshold leads to zero counts below threshold and then a turn on calibration curve described by the parameters c and t . Above this regime, there is a linear response described by the parameters a and b . The parameters of the surrogate function need to be measured experimentally. An obvious option is to use radiation of different energies. Typically one uses different radioactive sources and some fluorescence lines. Figure 3.11 shows such a measurement.

This calibration curve is valid until about 700 keV per pixel. At higher energies, there is an oscillation in the pre-amplifier leading to a certain transition region and at yet higher energies to another linear regime with larger slope, i.e. different fit parameters a and b ([76], [77]). A more precise energy calibration by more sophisticated data analysis is described in [78]. The calibration can be performed for each single pixel, allowing for correction of differences between pixels of the ASIC. Possible sharing

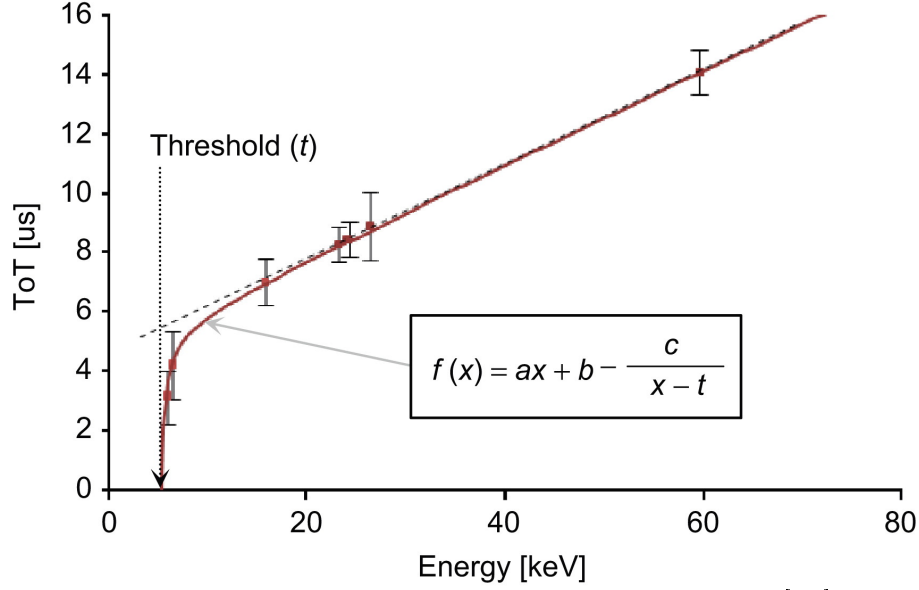


Figure 3.11: Energy calibration of a Timepix pixel [75].

of the charge between pixels is a problem for this calibration method. Especially in a gaseous detector like the GEMPix, the charge of basically any ionising particle is shared in many pixels. For example, a typical cluster resulting from 5.9 keV X-rays from ^{55}Fe is distributed over about 100 pixels, the exact value depending on the detector settings. Therefore this calibration method does not work for single pixel calibration in the GEMPix.

Another method is the use of built-in test pulses generated by the FITPix interface. A defined amount of charge is injected into single pixels. This method can at least in theory avoid the use of external radiation sources by calibrating the response of the pixels to the test pulses. This can obviously only correct differences in the ASIC and not in the sensor and does not give the conversion of TOT counts into energy but only performs a relative calibration. There are also other problems regarding the reliability at energies close to threshold, as reported in a comparison of different calibration methods [76].

3.2.8. Radiation Hardness

When the Timepix is exposed to radiation, detector performance deterioration and irreversible damage are expected, depending on instantaneous dose rate and total accumulated dose. An example of a reversible error is a Single Event Upset (SEU), which could be noticed as a bit-flip. Irreversible damage occurs after a cer-

tain amount of total accumulated dose. Typical are an increase of the noise level and at even higher accumulated dose the complete loss of pixels. Statements on the radiation hardness of the Timepix are often based on the experience gained with devices successfully operating under irradiation, for example an array of Timepix detectors for several years in the A Toroidal LHC ApparatuS (ATLAS) cavern [79] or Timepix detectors on board the International Space Station (ISS) [80]. An example for an evaluation of the radiation hardness can be found in [81], with requirements of 100 krad for the electronics and 1000 krad for the detector to launch Timepix devices on board a satellite. Few dedicated studies of the radiation hardness exist, such as [82] and [83]. In [84] small changes of the energy calibration of the pixels (see section 3.2.7) are reported after irradiation with only 6×10^9 protons/cm². However, most of the studies and stated numbers refer to the Timepix in combination with a silicon sensor. In these cases it is more likely that the sensor and not the ASIC is damaged first. Effects from the sensor and the ASIC are hard to disentangle in these studies but it can be assumed that the ASIC alone is more radiation tolerant. A study on the radiation hardness of the Medipix3 ASIC – which is expected to show an improvement by several orders of magnitude compared to Medipix2– shows that the Medipix3 ASIC is operating well even after irradiation of 460 Mrad [85].

3.2.9. Timepix Application Overview

The Medipix and Timepix ASICs have found many applications in various fields including educational purposes [86], space dosimetry [87], radon detection [88], characterisation of mixed radiation fields [89], proton and helium beam radiography [90] and other hadron therapy applications [91], X-ray imaging [92] and many others. A recent overview can be found in [73].

3.3. GEMPix

3.3.1. Introduction to the GEMPix Detector

The GEMPix detector (first published in [93]) consists mainly of three different parts: a gas detection volume of $2.8 \text{ cm} \times 2.8 \text{ cm} \times 1.2$ or 0.3 cm , three GEMs for gas amplification and four Timepix ASICs for readout. Note that only the Timepix ASIC is used here, not the combination with a silicon sensor. Figure 3.12 shows a picture of the GEMPix, figure 3.13 shows a scheme of the detector and the necessary electric fields and figure 3.14 shows a picture of the opened detector.

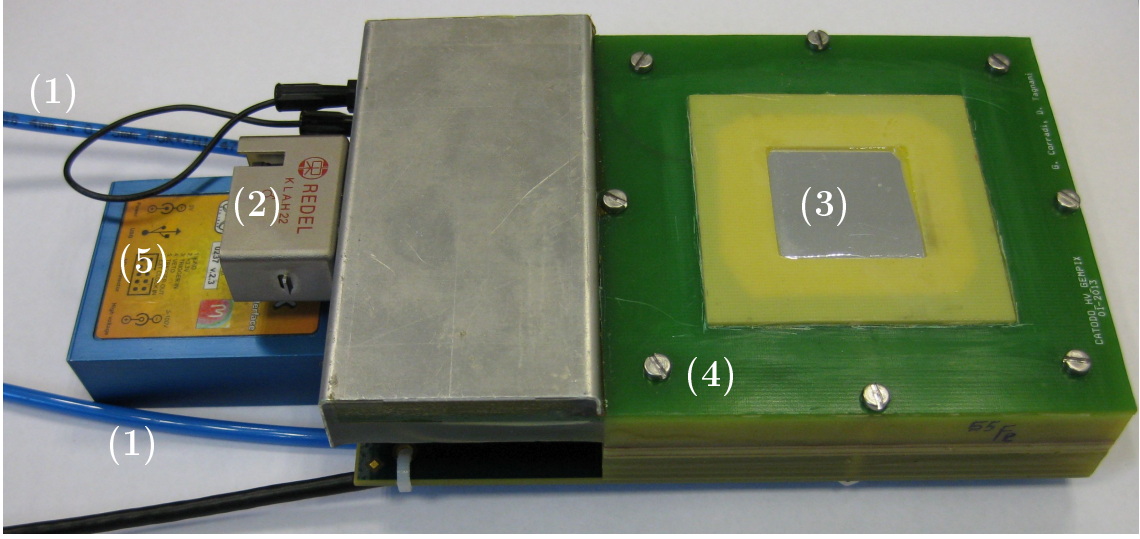


Figure 3.12: The GEMPix and the necessary periphery: (1) gas inlet and exhaust tubes, (2) HV connector, (3) thin Mylar entrance window, (4) frame to hold the GEM foils and (5) the FITPix readout.

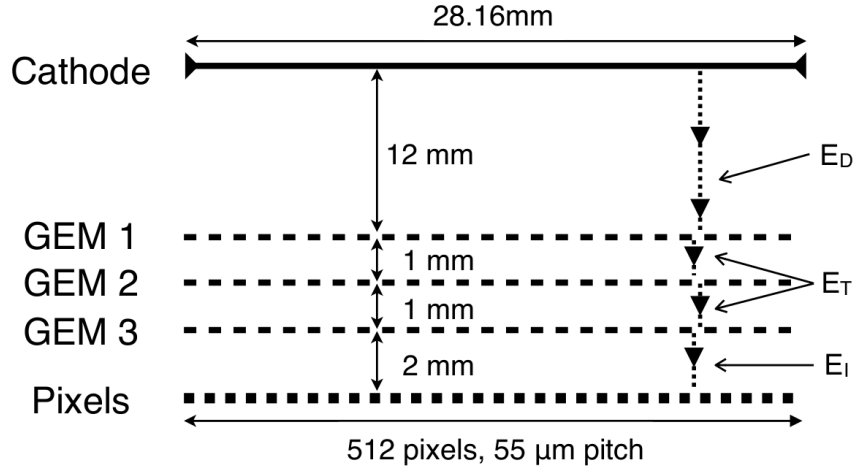


Figure 3.13: Schematics of the GEMPix and the applied electric fields in the GEMPix [24]. On the top, there is the Mylar entrance window followed by the drift field (E_D) in the detection volume, which height depends on the GEMPix configuration. Three electric fields are applied between upper and lower part of each GEM. Between the GEMs, two transport fields (E_T) drive the electrons to the next GEM. Finally, the induction field (E_I) guides the electrons from GEM3 to the readout pixels.

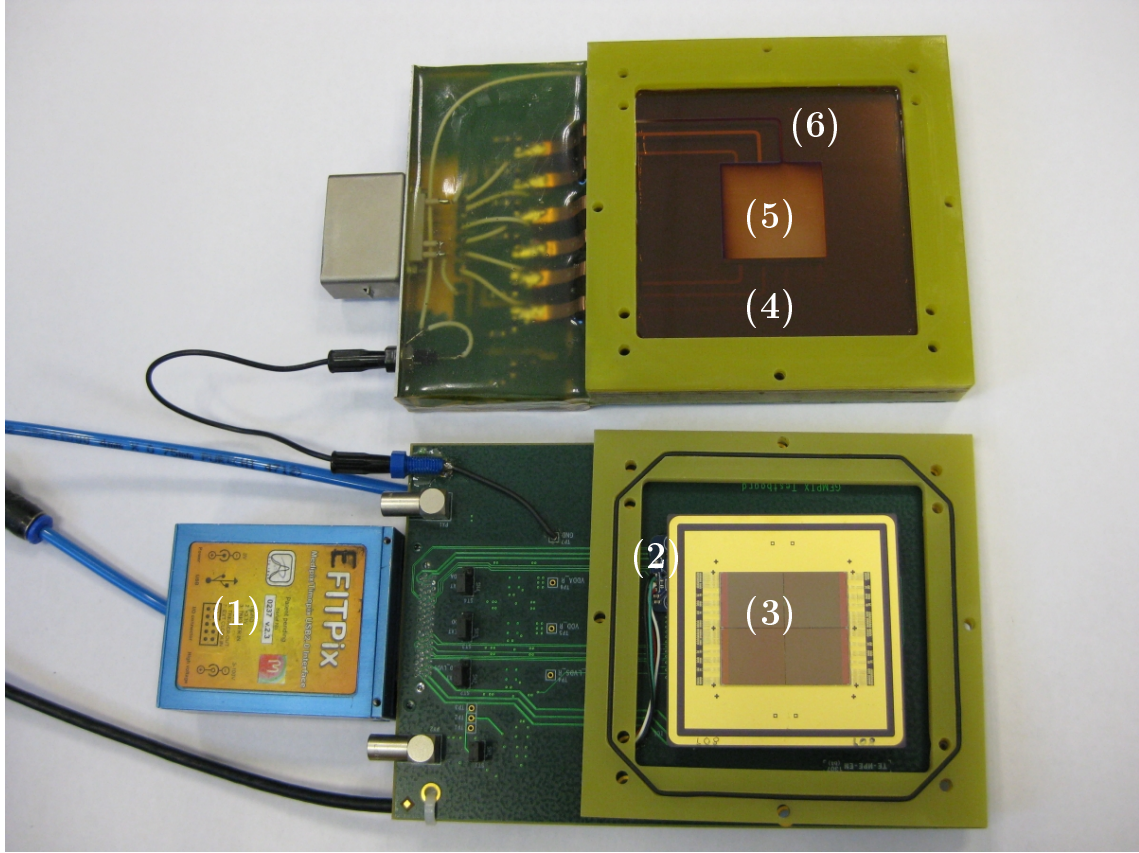


Figure 3.14: The opened GEMPix detector with the FITPix (1). The temperature, pressure and humidity sensor (2) is glued behind the board of the four Timepix ASICs (3). Only the centre of the Kapton foil (4) is prepared as a GEM and therefore covered with copper (5). This GEM foil shows a manufacturing problem, resulting in a violet colour (6). Most likely it is a passivation non-uniformity that can lead to a dielectric deposition during operation of the GEM.

The particles to be detected first need to pass through a less than 20 μm thin Mylar (polyethylene terephthalate) window. It is gas tight to confine the gas in the gas detection volume but thin enough to not stop low-energy particles⁽¹⁾. The gas is continuously flushed through the detector at a rate of typically 3 L/h to 5 L/h. The gas is guided through the inlet into a point opposite the HV connector. It then flows first through the GEMs towards the gas detection volume where the exhaust

⁽¹⁾The attenuation of 5.9 keV X-rays of ^{55}Fe in the entrance foil is less than 1‰. This value is calculated using equation 2.10 and the density and attenuation coefficient provided in the NIST online database [94], first published in [95].

pipe is located on the side closer to the HV connector. In this way a gas exchange in the whole detector is ensured. Gases like Ar:CO₂:CF₄ (45:15:40) are available in standard gas bottles. Pressure reduction to around 2bar is needed and the gas flow is adjusted and monitored with a flow metre.

A series of electric fields is needed to operate the GEMPix: electrons and ions in the detection volume are drifted into opposite directions by the drift field E_D ; gas amplification for the electrons takes place in the holes of the GEMs due to the high applied electric fields E_{GEM1} , E_{GEM2} and E_{GEM3} ; in between the GEMs there are transfer fields E_{T1} and E_{T2} to drift the electrons to the next GEM; the induction field E_I transports the electrons from the last GEM to the Timepix ASIC. Figure 3.13 shows the applied electric fields schematically.

It is not straightforward to power all the needed fields in a reliable and adjustable way. An HV module called HVGEM was developed at Istituto Nazionale di Fisica Nucleare (INFN) Frascati [96] and provides seven voltage channels, each equipped with a trip control. It is connected to the PC via an OpenCAN interface and a Kvaser USB CAN II adaptor. In this work a LabVIEW based control is used that provides the following features: setting and monitoring the voltages; measuring the currents driven by the fields; providing a trip control in case of too high currents driven; displaying the temperature, pressure and humidity values; calculating the online HV correction; writing the voltages, currents and slow control data to file. Figure 3.15 shows a screenshot of the control.

3.3.2. GEMPix Application Overview

The GEMPix has found applications in several fields: as a mini-TPC for particle tracking in high energy physics [24]; as a diagnostic tool for soft X-rays emitted by laser produced plasmas [97] and for studies on a negative ion TPC read by a GEMPix for dark matter research [98]. For medical applications, a few GEMPix prototypes have been built for use in proton tomography studies at Dutch National Institute for Nuclear and High Energy Physics (Nikhef). These detectors have shown a track position precision of 100 μ m and an angular precision of about 1° [99]. Some measurements have been made in Frascati (Italy) to test the capability of GEMPix as real time dosimeter in external photon beam radiotherapy ([100], [101]). In this work two other applications in the field of sample characterisation of radioactive waste (chapter 4) and in particle therapy (chapter 5) are presented.

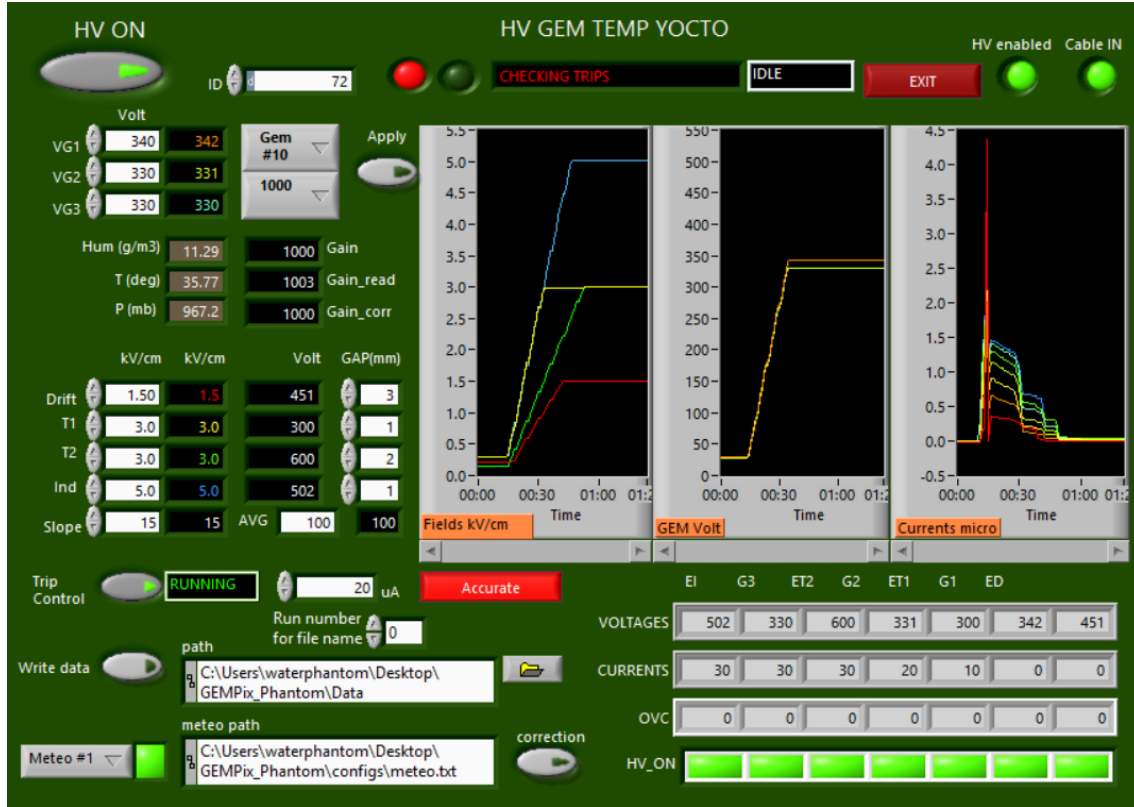


Figure 3.15: Screenshot of the LabVIEW GEMPix HV control. All voltages for the seven fields can be set and monitored as well as the slow control data (left side). The three plots show (from left to right): the voltages of the drift, transfer and induction fields against time; the voltages of the three GEMs against time; the currents driven by all fields against time. The temperature, pressure and humidity values are displayed (left side).

3.4. Detector Characterisation

3.4.1. Gain Scans with ^{55}Fe

Finding the good gain setting for example for measurements with an ^{55}Fe source is possible by a gain scan: the sum of the GEM gas amplification voltages and thus the gain is changed and the evolution of certain parameters is observed. The minimum gain is chosen so low that no signal is observed while the maximum gain is typically around 1350 V to avoid larger risk of discharges at even higher gains. The rate of the ^{55}Fe source is chosen such that single clusters are well distinguishable – a good

value is typically around 20 clusters per frame – and therefore the first quantity of interest is simply the number of clusters.

Figure 3.16 shows the typical S-shape with no counts below a certain voltage and then a smooth transition towards a stable plateau, which can be fit by an integrated Gaussian function. The TOT response to the deposited energy⁽²⁾ shows the expected exponential dependence only at gains still larger than the start of this plateau (figure 3.17), a fact that is related to the transparency (section 3.1.6). Figure 3.18 shows the resolution, defined as the full width at half maximum (FWHM) of the measured ⁵⁵Fe peak divided by the mean peak position μ . Gain scans with other sources are also possible and results are presented in the appendix (see sections A.2 and A.3). For all these figures, an estimated uncertainty of 1 V is assigned to the sum of the GEM voltages. The uncertainty on the number of clusters in figure 3.16 is the ‘counting uncertainty’⁽³⁾, while the uncertainty on the TOT counts and the FWHM is obtained from the Gaussian fit to the measured ⁵⁵Fe spectrum.

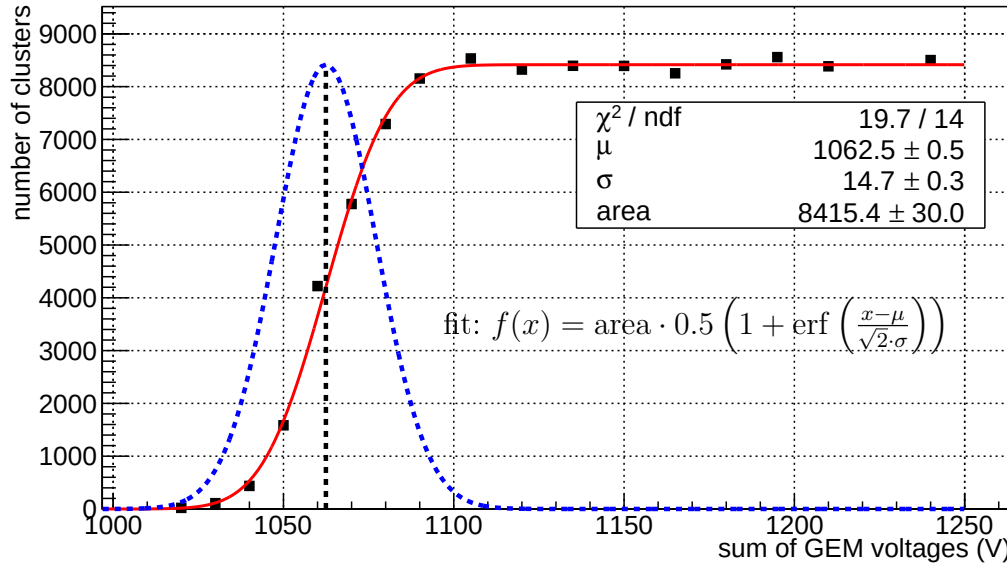


Figure 3.16: Gain scan with an ⁵⁵Fe source: the number of clusters against the total gain voltage (black) are fit well by an integrated Gaussian function (red solid line). The derivative of the fit function (i.e. a Gaussian function, blue dashed line) is drawn for comparison, with the vertical black dashed line showing the mean value at which 50% of the events are detected. Error bars are smaller than data points.

⁽²⁾Defined here as the mean value of a Gaussian fit to the ⁵⁵Fe peak in the TOT spectrum.

⁽³⁾Sigma is equal to the square root of the number of events.

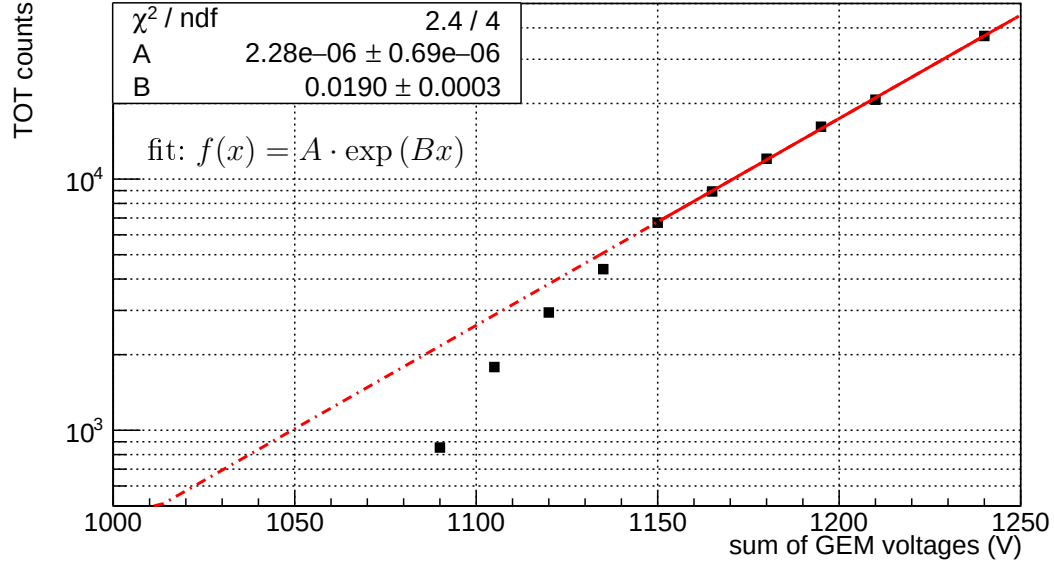


Figure 3.17: Gain scan with an ^{55}Fe source: the mean TOT values for each gain against the total gain voltage (black) are fit well by an exponential function (red) above 1150 V. Note that the linear regime is only reached for higher gain than the beginning of cluster count plateau (compare with figure 3.16). Error bars are smaller than data points.

It is possible to extract the applied threshold in terms of energy from the presented gain scan. The mean value of the fitted Gaussian function in figure 3.16, 1062 V, corresponds to the gain at which 50% of the 5.9 keV X-rays lead to a signal passing the threshold while the other 50% remain undetected. The expected energy threshold thl at a certain voltage U is calculated by:

$$thl = 5.9 \text{ keV} \frac{f(1062 \text{ V})}{f(U)}, \quad (3.8)$$

using the fit function $f(x)$ in figure 3.17. For the typical voltage used for measurements with ^{55}Fe (1240 V), this yields about 200 eV. However, for the typical voltage used at CNAO (990 V), this yields about 130 keV⁽⁴⁾.

⁽⁴⁾Note that these values are rough estimates. The exact value also depends for example on the temperature and pressure effects introduced in section 3.4.5 and is larger if all events and not only 50% of the events should be above threshold.

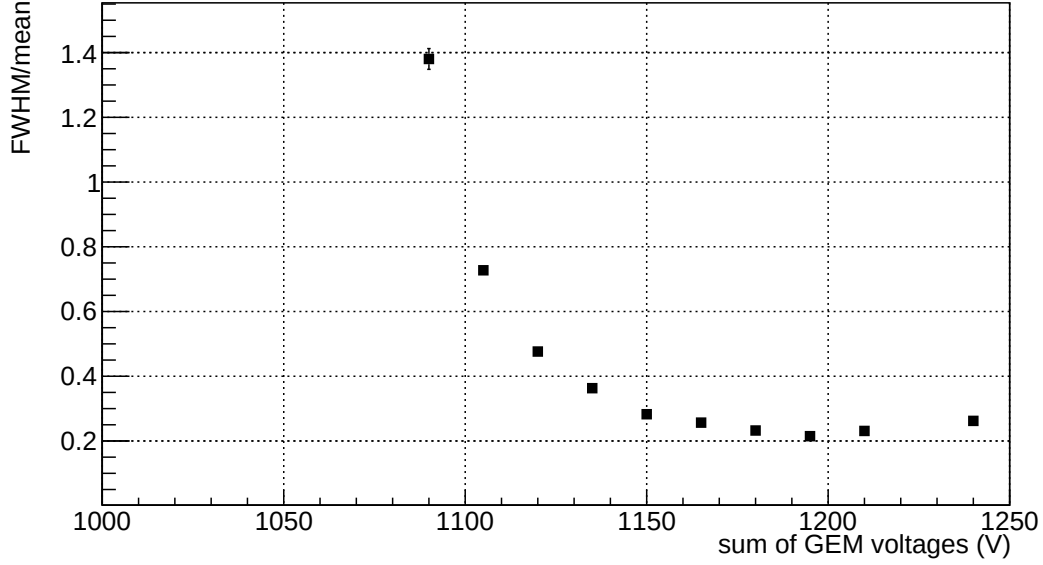


Figure 3.18: Gain scan with an ^{55}Fe source: the resolution (defined as the FWHM divided by the mean TOT values) improves for higher gain and reaches a plateau above 1180 V. Error bars of most measurements are smaller than data points.

3.4.2. Spatial Gain Distribution

Differences in the response over the instrumented area do not only depend on the pixels but also for example on the electric field homogeneity or differences between the four Timepix ASICs. Measurements with an ^{55}Fe source can reveal these differences and can be used to develop a correction. Pixels are grouped in so-called superpixels of typically 16×16 pixels each. The peak position of the 5.9 keV-peak in each superpixel is determined and the ratio to the expected 5.9 keV used as a correction map. Maximum and minimum value of the correction over the whole sensitive area differ typically by a factor of approximately 1.5. Figure 3.19 shows results of a measurement after application of the correction. The correction works well as all values are within 5950 ± 200 TOT counts.

3.4.3. Response to Different Fitpix Clocks

A measurement with different Fitpix clocks is performed to check if the GEMPix response increases linearly with the clock speed. This is important to know when adjusting the clock settings for measurements for example at CNAO. The TOT

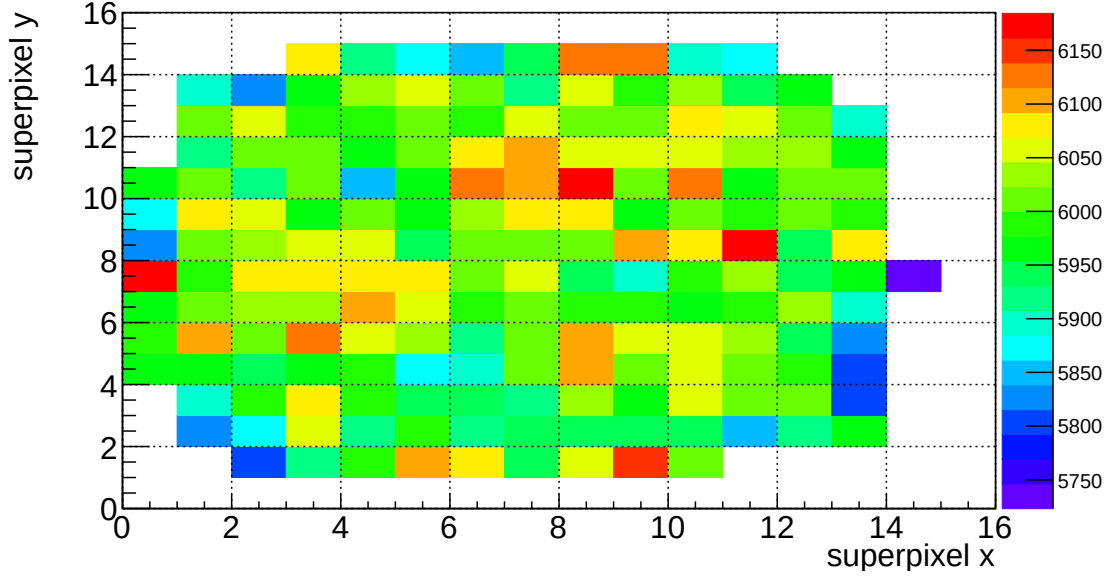


Figure 3.19: Spatial distribution of the mean TOT values (colour coded) in the superpixels. Superpixels without a value have not received enough statistics (^{55}Fe source placed close to the centre).

response to the approximately 3 and 6 keV X-rays of ^{55}Fe is obtained from Gaussian fits to the energy spectrum at different clock speeds. A linear response is indeed observed and the ratio of the two peaks stays constant (figure 3.20). It should be noted that this test only holds for good gain settings. If the signals are close to the detection threshold and the response is only a few counts, the dependence will not be linear. This is of interest for measurements at CNAO, where also very small signals can occur. Uncertainties on the TOT value are obtained from the Gaussian fits.

3.4.4. Effects When Switching on the GEMPix

The GEMPix needs to be turned on in advance before a measurement to allow for stabilisation of the detector response. The time needed for stabilisation of the GEMPix response differs between the different preparatory actions like starting the gas flow and is presented in the following. Measurements in this section are performed with an ^{55}Fe source. TOT values and their uncertainties are obtained from Gaussian fits to the energy spectrum at different times after the start of the measurement.

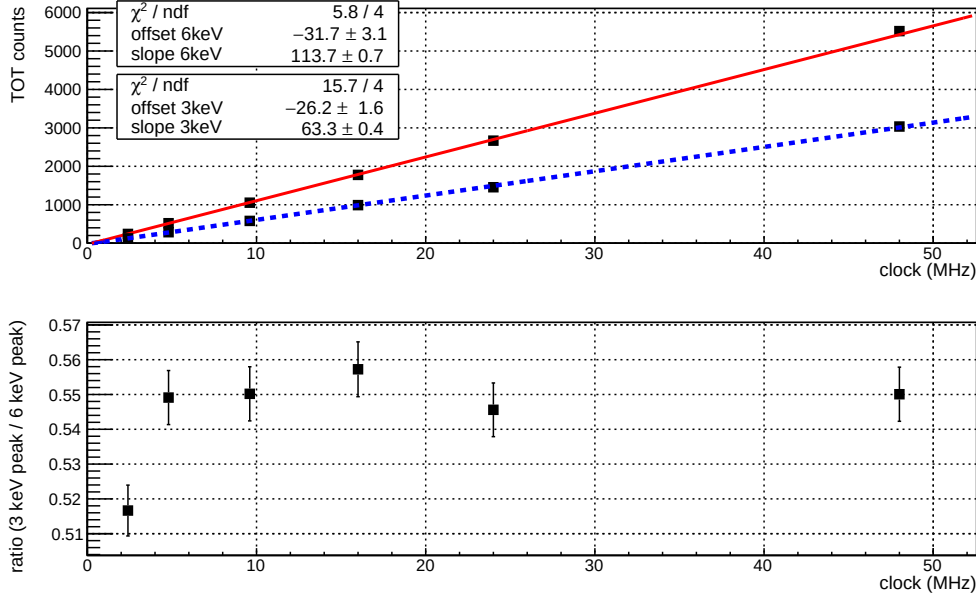


Figure 3.20: The mean values of the approximately 6 keV (upper plot, red solid line fit) and the 3 keV peak (upper plot, blue solid line fit) of ^{55}Fe depend linearly on the clock. The ratio between both (lower plot) stays constant as expected.

Starting the Gas Flow

It takes some time for the detection gas to flush out the air present in the GEMPix. Typically this time is about 20 min when a gas flow of 4 L/h is used. Figure 3.21 shows the result of a measurement with ^{55}Fe . First the measurement is started at the same time as the gas flow and the TOT counts of the ^{55}Fe peak are measured until a stable value is reached. In order to ensure that this effect can be assigned to the gas flow, the gas flow is stopped again for some time to allow for the ambient air to enter the detector. Then the GEMPix is flushed again with gas until a stable response is reached. The HV stays on during the entire measurement to avoid any effects due to changes in the HV (see next paragraph).

Turning the HV on

The main build-up of the electric field is fast and follows directly the ramping up of the HV: the HV is ramped up within about one minute and the currents driven by the fields reduce significantly as soon as a stable voltage is reached. However, there is an effect when turning the HV on probably due to charge up (see section 3.1.6).

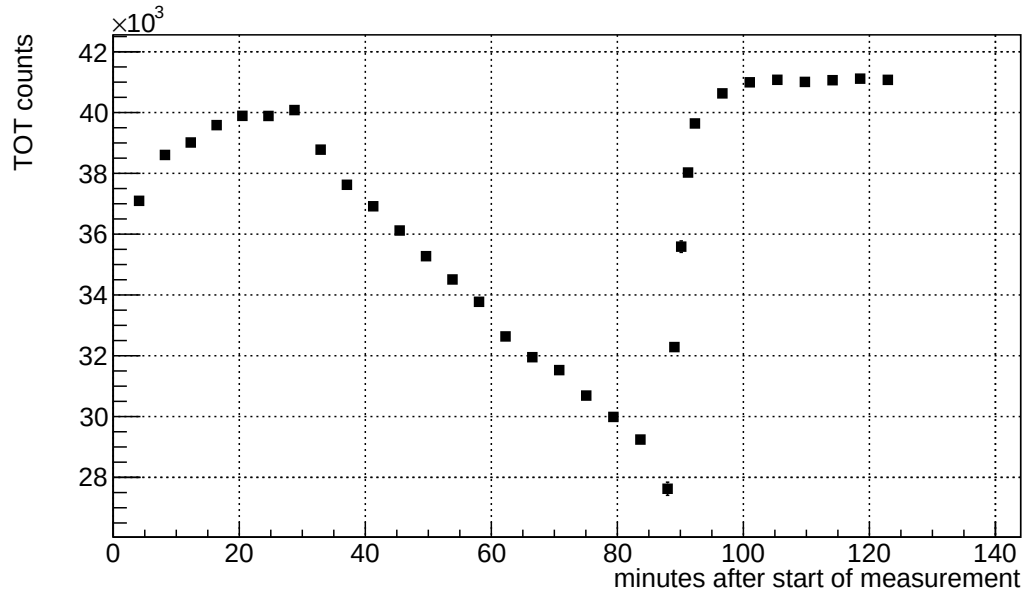


Figure 3.21: The gas flow is started (minute 0) after no measurements were performed for a long time and the response stabilises after about 20 minutes. Then the gas valve is closed (minute 30) and the response decreases until the valve is opened again (minute 90) and the response stabilises again at a slightly higher plateau value (minute 100). Error bars are smaller than data points.

Another effect could be a small movement of the GEM foils which is however more likely when the gas flow is started. Figure 3.22 shows that it takes approximately 40 min until a stable gain plateau is reached after the HV has been ramped up.

Temperature Change

The gas temperature has a major impact on the detector response (see section 3.4.5). Besides typically slow changes of the ambient temperature there is a fast effect due to the power consumption of the Timepix chips and the unavoidable heat production. This fast heat-up of the Timepix ASICs is also transferred to the gas as they are in direct contact with it. The powering of the GEMPix with the low voltage (LV) heats up the GEMPix to about 35°C within approximately 30 min (with the exact value depending on the ambient temperature).

Another heat-up occurs when the detector is irradiated and read out. The exact duration and size of this heat-up depends on the read-out frequency and also the ambient temperature. Typical values are 2°C temperature increase in about 15 min.

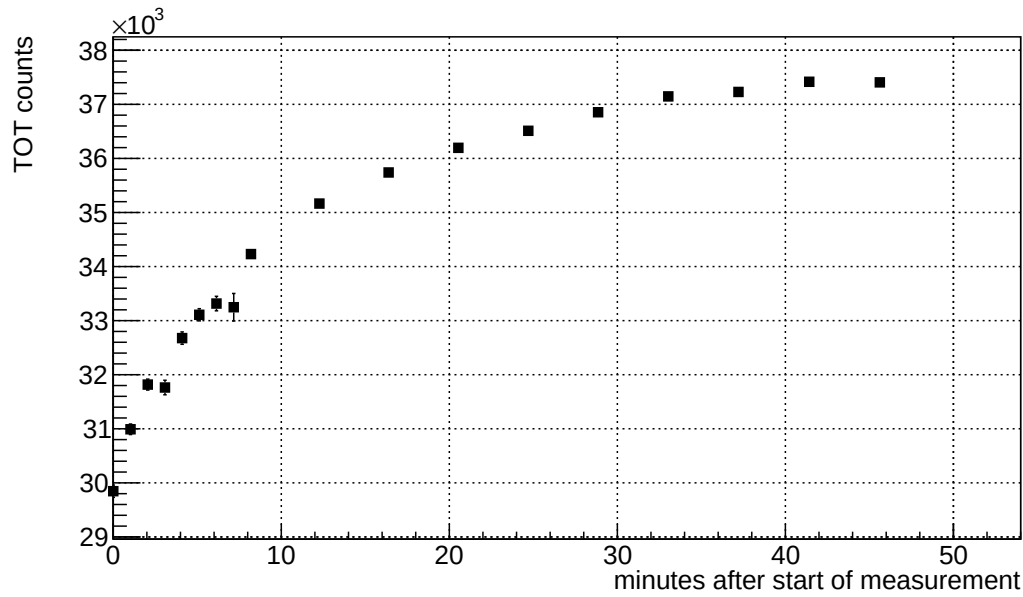


Figure 3.22: The HV is turned on (minute 0) and the detector response stabilises after about 40 min. The gas has been flowing for three hours before to ensure that the observed effect can be clearly assigned to the HV. Error bars are smaller than data points.

After the stated time periods, a stable temperature equilibrium and therefore a stable detector response is reached.

Avoiding Effects When Switching on the GEMPix

The best way to avoid problems with the effects presented above is to turn on the GEMPix some time before a measurement. Ideally the detector is flushed with gas over night before a measurement. Of course, the HV and LV should be turned on at the same time but since the stabilisation time is smaller in this case, it is not a problem to slightly adjust the gain right before a measurement. The only effect that cannot be completely avoided is the heat-up due to the readout. A good strategy that is implemented for measurements at CNAO, is to read out the GEMPix even when the actual measurement has not yet been started. In this way the heat-up is further reduced. However, the remaining effect should be corrected for or at least monitored as presented in section 3.4.5.

3.4.5. Humidity, Temperature and Pressure Correction

The detection gas in the GEMPix needs to be well monitored as it is the case for any gaseous detector. A sensor (Yocto-Meteo by Yoctopuce company [102]) measuring temperature, pressure and humidity is installed inside the gas on the GEMPix board⁽⁵⁾. Figure 3.14 shows the sensor mounted on the board. This section was partially published in [103].

Online Temperature and Pressure Correction

First, the dependence of the TOT counts on temperature T and pressure P in the gas has to be understood. Therefore data with a fixed HV at different temperature and pressure values are acquired with an ^{55}Fe source⁽⁶⁾. Figure 3.23 shows the result and a fit of an exponential function to it. Uncertainties on most TOT-values are around 1%, only for some data points they are much larger due to measurements with a fast heat-up (see paragraph on temperature changes in section 3.4.4) which leads to a large spread of TOT values in this T/P -bin. The exponential function is expected as the First Townsend coefficient α is proportional to T/P and therefore the gain depends exponentially on T/P (see for example in [48] and the generalised form of equation 2.24 ⁽⁷⁾):

$$TOT = p_0 \exp(p_1 T/P) \quad (3.9)$$

where p_0 and p_1 are the fit parameter obtained from the fit in figure 3.23.

An active HV correction is advantageous because the constant gain results in a stable number of electrons per ionisation and therefore the same effect of the threshold applied to the Timepix pixels. Note that the threshold cut is irreversible and the information is lost, i.e. the threshold cut cannot be changed offline. Only the digitised signal after the threshold cut is available. In order to correct the HV online, the dependence of the TOT counts on the HV has to be measured. As shown in equation 2.26, the gain (and therefore the TOT value) can be adjusted by changing the applied HV. The data taken with an ^{55}Fe (figure 3.17) and an ^{241}Am source (figure A.3) are divided by the corresponding deposited energy and combined in figure 3.24 (the energy of the α -particles after the attenuation in air and the entrance

⁽⁵⁾In the following it is assumed that the measured values are uniform in the gas volume since mainly slow variations are of interest here.

⁽⁶⁾Temperature, pressure and humidity are only monitored but could not be adjusted systematically. Changes in the conditions in the detection gas are due to changes in ambient conditions, heat produced by the readout electronics and residual humidity when turning on the gas flow.

⁽⁷⁾In the generalised form, equation 2.24 does not only depend on the pressure but on the gas density at a certain pressure and temperature.

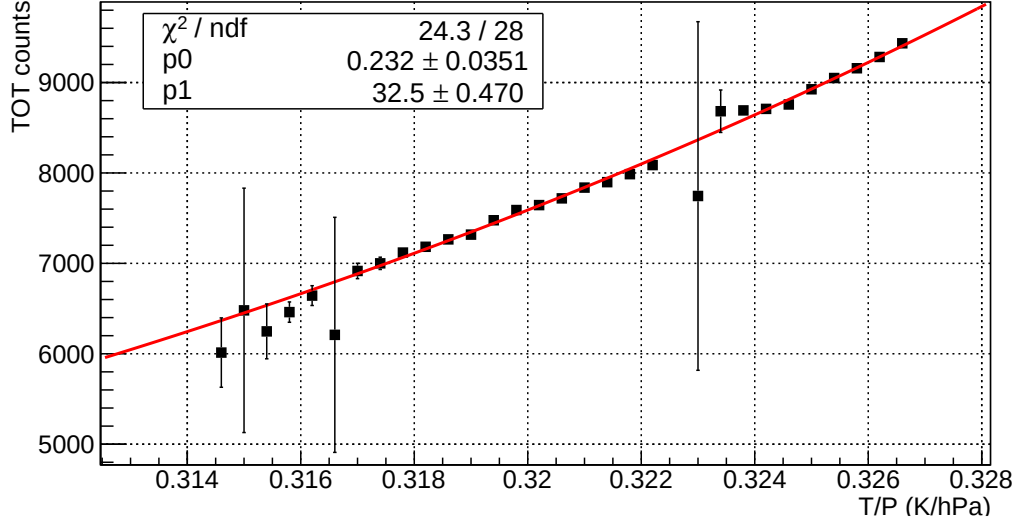


Figure 3.23: TOT counts of the GEMPix at different temperature and pressure values are obtained from Gaussian fits to the TOT spectra. The mean values show the expected exponential dependence on the ratio of temperature and pressure (T/P). Similar plot in [103].

window is around 800 keV). The plot shows the expected exponential dependence of the TOT value (here called TOT_{set} to stress the fact that this can be chosen by adjusting the gain):

$$TOT_{\text{set}} = A \cdot \exp(BV_{\text{set}}) \quad (3.10)$$

where A and B are the fit parameters in figure 3.24⁽⁸⁾.

Equation 3.9 can be rewritten as:

$$TOT(V_{\text{set}}, T/P) = TOT_{\text{set}} \cdot p'_0 \cdot \exp(p_1 T/P) \quad (3.11)$$

where p'_0 is a new constant derived from p_0 . The goal is to choose $V_{\text{set}} = V_{\text{TP corrected}}$ such that $TOT(V_{\text{set}}, T/P) = \text{const.}$ Equation 3.10 is inserted in equation 3.11 and solving for V yields:

$$V_{\text{TP corrected}} = \frac{1}{B} \ln \left(\frac{\text{const.}}{p'_0 A} \right) - \frac{p_1}{B} \frac{T}{P}. \quad (3.12)$$

⁽⁸⁾Since the measurements are performed with two different energies (^{55}Fe and ^{241}Am sources), the TOT value in figure 3.24 is normalised to the energy. However, this normalisation factor would be absorbed in the constant part of equation 3.12 and is therefore neglected here.

The first part in equation 3.12 is constant and therefore equation 3.12 can be rewritten as:

$$V_{\text{TP corrected}} = V_{\text{uncorrected}} + C - \frac{p_1}{B} \frac{T}{P} \quad (3.13)$$

where $V_{\text{TP corrected}}$ is the applied corrected voltage, $V_{\text{uncorrected}}$ is the uncorrected voltage and C is a new constant combining constants introduced above such as A .

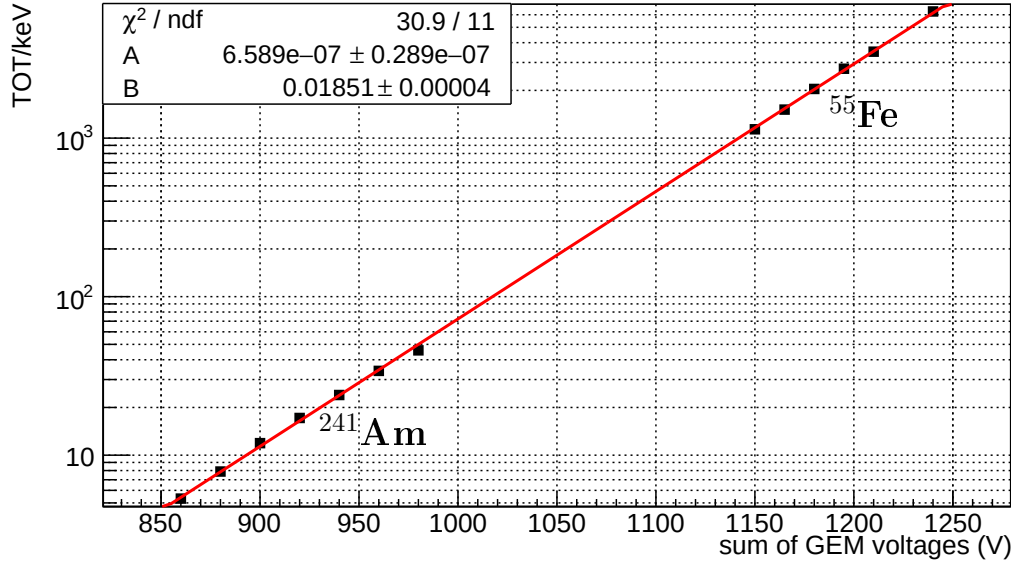


Figure 3.24: TOT counts of the GEMPix at different gains are obtained from Gaussian fits to the TOT spectra. They show the expected exponential dependence on the sum of the GEM voltages (similar plot in [103]). Measurements are performed with an ^{241}Am source and an ^{55}Fe source (see also figures A.3 and 3.17).

Online Temperature, Pressure and Humidity Correction

It is noticed that in data acquired with an actively corrected HV according to equation 3.13, a systematic linear dependence on the humidity in the gas exists. Figure 3.25 shows a measurement with applied T/P correction and a linear fit to the data:

$$\text{TOT} = p + qH \quad (3.14)$$

where p and q are the fit parameters shown in figure 3.25 and H is the measured humidity in the gas.

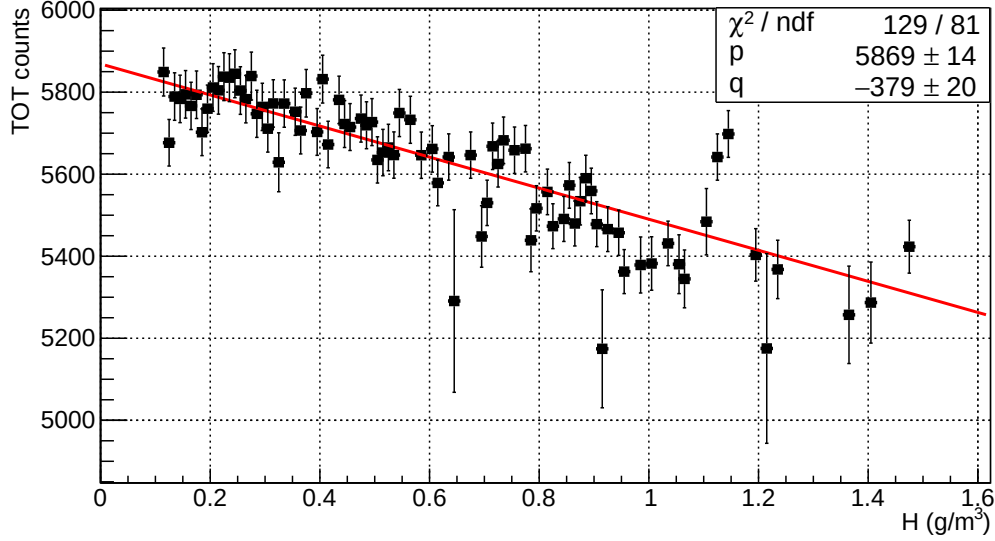


Figure 3.25: TOT counts of the GEMPix at different humidity values are obtained from Gaussian fits to the TOT spectra. They show a linear dependence on the humidity when applying an online HV correction for effects of temperature and pressure (equation 3.13).

Typically the humidity is high only soon after starting the gas flow. It is unclear if the observed effect is related to the humidity or maybe to other gas impurities that are also flushed away when starting the gas flow. Nevertheless a correction formula was developed with equations 3.10 and 3.14, using the same approach as for the T/P correction:

$$\text{const.} \stackrel{!}{=} TOT = TOT_{\text{set}} (p' + q'H) \quad (3.15)$$

$$= A \exp(BV_{\text{set}}) \cdot (p' + q'H) \quad (3.16)$$

$$\Rightarrow V_{\text{set}} = \frac{1}{B} \left[\ln \left(\frac{\text{const.}'}{A} \right) - \ln(p + qH) \right] \quad (3.17)$$

where p' , q' and $\text{const.}'$ are new constants derived from p , q and const. ⁽⁹⁾.

Simplifying the second term by Taylor expansion by assuming $q/p \cdot H \ll 1$, yields⁽¹⁰⁾:

$$\ln(p + qH) = \ln(p) + \frac{q}{p}H + \mathcal{O}(H^2). \quad (3.18)$$

⁽⁹⁾For example: $p = TOT_{\text{set}} \cdot p'$.

⁽¹⁰⁾For example for a humidity of 1 g/m³ the measured values for $q/p \cdot H$ is about 0.06. The values are closer to 1 for a higher humidity. However, the resulting final correction formula is tested experimentally and results in a stable detector response (see figure 3.26).

The final correction formula then is:

$$V_{\text{HTP corrected}} = V_{\text{TP corrected}} + C' - \frac{q}{Bp}H \quad (3.19)$$

$$\Rightarrow V_{\text{HTP corrected}} = V_{\text{uncorrected}} + C'' - \frac{p_1}{B} \frac{T}{P} - \frac{q}{Bp}H \quad (3.20)$$

where C' and C'' are new constants combining other constants introduced above such as A . For the measurements presented in figures 3.23, 3.24 and 3.25 this results in:

$$V_{\text{HTP corrected}} = V_{\text{set}} + C'' - (1755 \pm 26) \text{ V hPa/K} \frac{T}{P} + (3.5 \pm 0.1) \text{ Vm}^3/\text{gH}. \quad (3.21)$$

For measurements presented in this work, values resulting from an earlier analysis as presented in [103] are used:

$$V_{\text{HTP corrected}} = V_{\text{set}} + 538 \text{ V} - (1709 \pm 7) \text{ V hPa/K} \frac{T}{P} + (2.6 \pm 0.1) \text{ Vm}^3/\text{gH}. \quad (3.22)$$

The value of the constant C'' is determined in terms of an energy calibration such that e.g. applying $V_{\text{HTP corrected}}$ for measurements at certain ambient conditions with an ^{55}Fe source yields 5900 TOT counts. Uncertainties on fit parameters are obtained from the fit routines and propagated on the final quantities. The uncertainties in equation 3.22 are underestimated (see [103]). The results in equations 3.21 and 3.22 for the T/P-correction are compatible within two standard deviations while there is a large relative difference in the humidity correction. However, the absolute resulting difference in the range of small humidities (less than 1 g/m^3) is less than 1 V.

This online correction in equation 3.22 has been checked to work well in a dedicated measurement lasting more than a week. Figure 3.26 shows that the GEMPix response to the 5.9 keV X-rays of an ^{55}Fe source is stable within $\pm 3\%$. As mentioned above, changes in the humidity, temperature and pressure values are due to changes in ambient conditions, heat produced by the readout electronics and residual humidity when turning on the gas flow.

Mix of Offline and Online Humidity, Pressure and Temperature Corrections

The use of an online HV correction also has a disadvantage: the smallest step size of the HVGEM is 1 V which has already an impact on the TOT response. A change of 1 V can correspond to a change of some percent, the exact value depending on the measurement settings. The active HV control is therefore not always used but a combined offline and online procedure is preferred. Before a measurement the

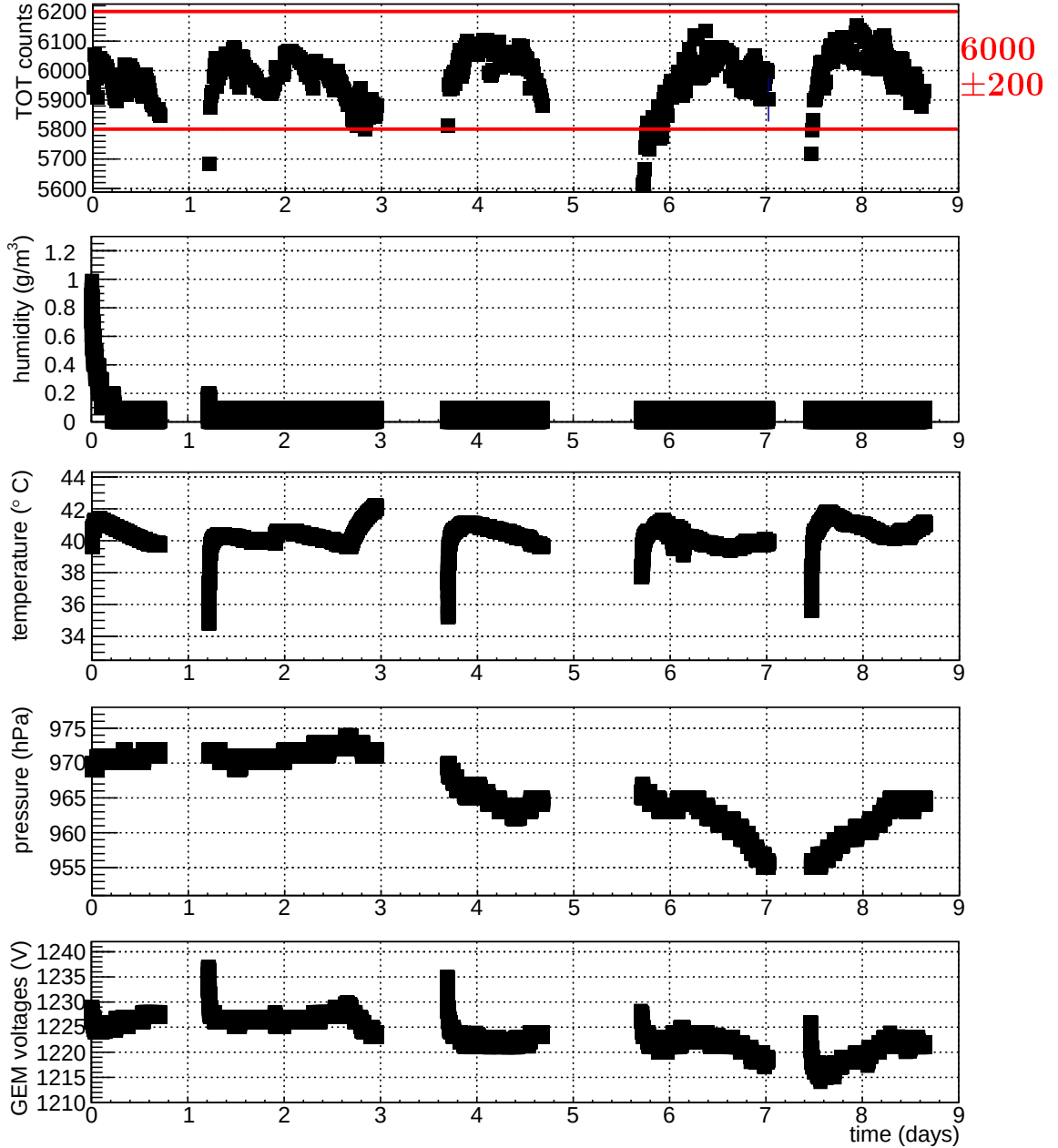


Figure 3.26: When the online HV correction is applied, the detector response (upper most plot) for a measurement with an ^{55}Fe source is stable within $\pm 3\%$ over more than a week (red lines: 6000 ± 200 TOT counts), except for periods with a very fast changing temperature due to the heat-up. The second through fourth plots show the change of the slow control data humidity, temperature and pressure. The bottom plot shows the HV changes due to the online correction. The HV was turned off completely between the third and the fourth and between the fourth and the fifth measurement periods (around day five and day seven).

voltage is set to the corrected value calculated in equation 3.22 but then no further active correction during the measurement is applied. For the measurement time, possible changes in the ambient conditions are typically small at least for short measurements and are in any case corrected offline. In this way an almost constant gain is reached for the measurements but steps in the response change are avoided by correcting small changes offline after the measurement. Starting from equation 3.22, using equation 3.10 and solving for TOT yields:

$$TOT_{\text{HTP corrected}} = C''' \exp \left(B \left(-1709 \text{ V hPa/K} \frac{T}{P} + 2.6 \text{ Vm}^3/\text{gH} \right) \right) \quad (3.23)$$

where C''' is a new constant. This correction formula is used for the measurements at CNAO presented in section 5.7. The constant C''' can be ignored for measurements at CNAO as measurements are only relative and a general normalisation factor is chosen in a later step of the analysis (see section 5.7.6).

3.4.6. Test with UV LED: Delay Time in the GEMPix

Signals produced by room light have been observed before in the GEMPix detector when using high gain, i.e. approximately above 1300 V [27, p. 130]. A simple test with the room light clearly shows the sensitivity of the GEMPix to the room light. However, it was suspected but not clearly understood that the signal is due to the UV component of the room light. A test with an ultraviolet (UV) light-emitting diode (LED) is performed to understand the signal production by UV light in the GEMPix and to measure possible delay times in the GEMPix. The latter is especially important for the water phantom set-up, as it relies on synchronous data acquisition of the detectors (see section 5.4.1). An external trigger is used to start the GEMPix data acquisition and to turn the UV LED on.

Measurement Set-up

A Vishay [104] indium gallium nitride (InGaN) LED is used (VLMU3500-385-060). Its wavelength ranges between 380 and 390 nm with the peak at 385 nm. Forward voltage should be 3.4 V with a forward current of maximum 700 mA. Typical voltage rise times for this type of LED are 100 ns to 200 ns [105]. A measurement shows a rise time of approximately 100 ns. The LED is placed in a few centimetres distance from the Mylar entrance window of the GEMPix. Other light sources are turned off. Figure 3.27 shows the set-up. An external trigger system is set up in order to be able to trigger both LED and GEMPix data acquisition, and delay either one of the

triggers. Possible delay for the LED is produced by a pulse generator, while for the GEMPix the delay can be set in the software.

For these measurements, the GEMPix is measuring in TOA mode to obtain the time spectrum. Each LED pulse is $25\mu\text{s}$ long and the trigger rate is 20 Hz. The internal clock of the GEMPix is set to 48 MHz, giving 20.8 ns per count for each pixel. Clock ticks are converted into time such that the results are given in units of time with t_0 at the start of a frame. Both, delay of the GEMPix data acquisition trigger and delay of the LED pulse are tested to work well.

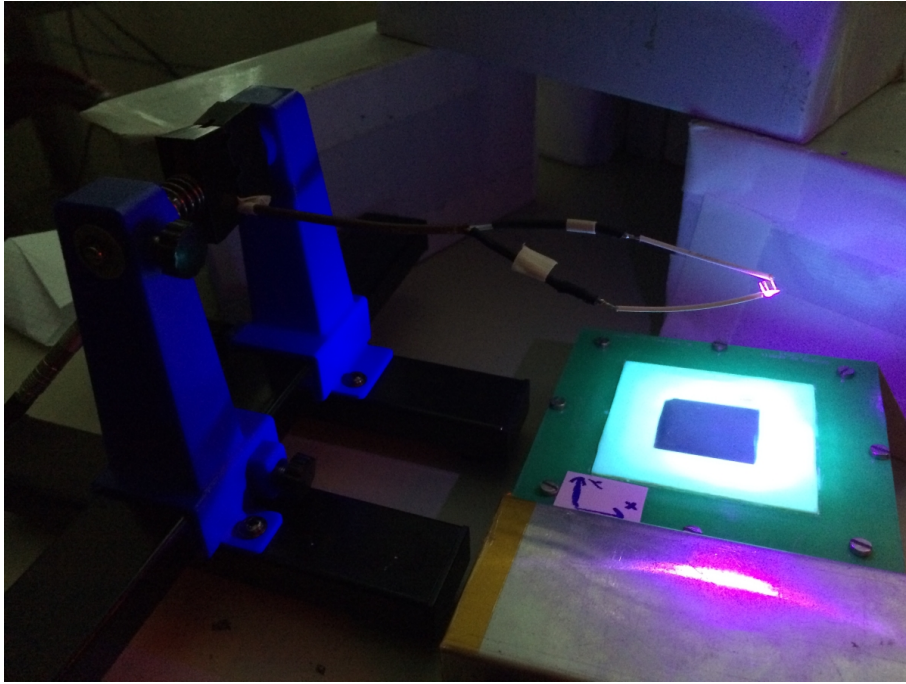


Figure 3.27: The emission of the UV LED is directed towards the Mylar entrance window of the GEMPix.

Measurement and Results

In order to obtain enough statistics the measurement lasts overnight. The frame length is adjusted properly to the maximum count of the pixels, i.e. $246\mu\text{s}$ ⁽¹¹⁾. A delay of the LED of $5.15\mu\text{s}$ is set in order to ensure that the start of the LED pulse is observed (which would not be the case if there was a significant delay of the GEMPix DAQ start after receiving an external trigger). The exact choice of the

⁽¹¹⁾The counter stops at 11810 counts which converts into $246\mu\text{s}$ at a clock frequency of 48 MHz.

delay is arbitrary; here $5.15\mu\text{s}$ is chosen. Figure 3.28 shows the result. The set pulse length of $25\mu\text{s}$ is well reproduced: a length of $24.6\mu\text{s}$ is measured. There is some uncertainty due to the rise and fall time of the LED of $0.1\mu\text{s}$ each, and due to the determination of the pulse length in the results⁽¹²⁾.

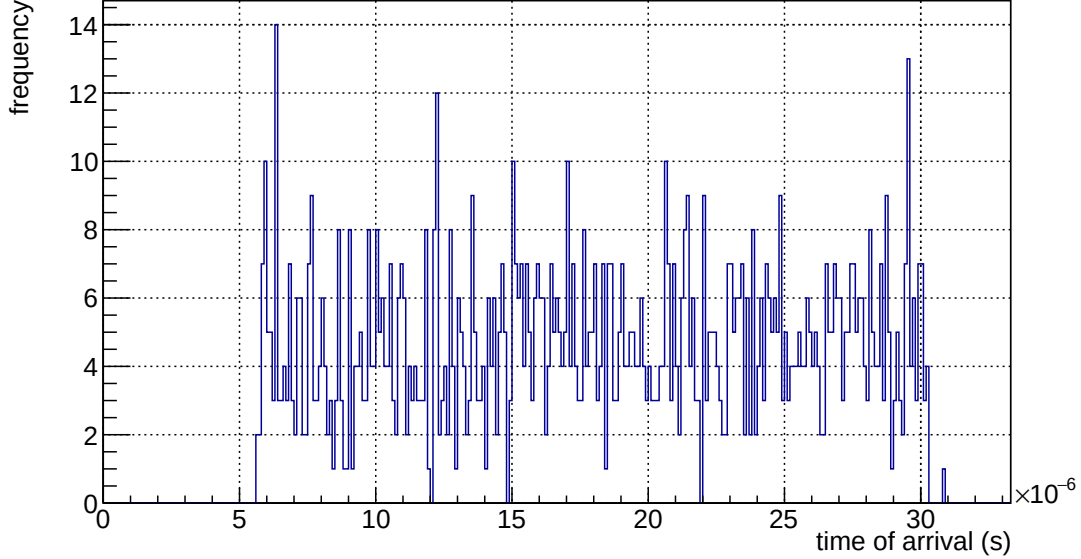


Figure 3.28: Timing measurement with the UV LED reproduce well the set delay time of $5.15\mu\text{s}$ and the set pulse duration of $25\mu\text{s}$. About 1200 signals are recorded in total.

A more detailed analysis is possible with a zoom to the data as shown in figure 3.29. Until the first photons are measured in the GEMPix, some time passes by:

- The set delay of $5.15\mu\text{s}$.
- The LED rise time of $0.1\mu\text{s}$.
- The drift time of the electrons in the gas detection volume of the GEMPix of $0.03\mu\text{s}$.
- The drift time of the electrons in the triple GEM zone of approximately $0.03\mu\text{s}$.
- A delay of 0.1 to $0.2\mu\text{s}$ until the first signals really arrive. Its origin is unknown.

Drift times are calculated based on drift velocity measurements [24]: the drift velocity at 1.1 kV/cm in the gas detection volume is equal to $4.1\text{ cm}/\mu\text{s}$. This yields $0.03\mu\text{s}$

⁽¹²⁾It is for example not clear when exactly the first UV photons are emitted when powering up the LED.

for a gap of 1.1 mm. A very approximate estimation for the triple GEM zone yields $12 \text{ cm}/\mu\text{s}$ at $3 \text{ kV}/\text{cm}$. This results in $0.03 \mu\text{s}$ for the 4 mm gap of the triple GEMs.

The nominal delay of the FITPix is 70 ns [33]. The method reported here is not sensitive enough to test that. There is an uncertainty of easily some 10 % in the calculations and measurements presented above, resulting in total to an estimated $0.1 \mu\text{s}$. However both arguments are not relevant for the purpose of these measurements: the signal production by the room light in the GEMPix is better understood and there is no significant delay of the GEMPix data acquisition after receiving an external trigger when the relevant time scale – the frame length – is milliseconds. This is the case for the set-up of the GEMPix and the reference ionisation chamber in the integrated water phantom system for measurements of the energy deposition in water by clinical ion beams.

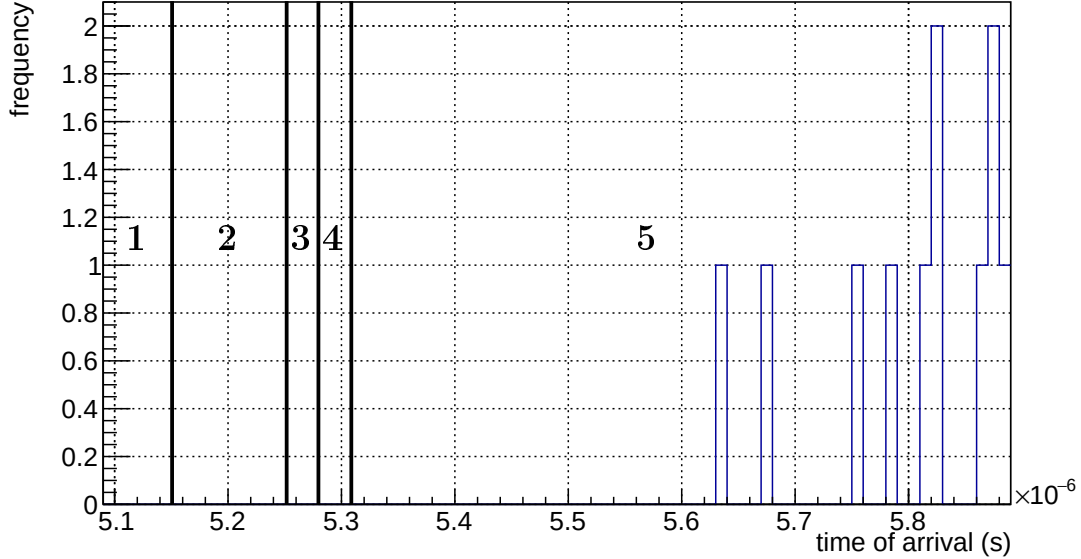


Figure 3.29: Zoom to the timing measurement with the UV LED in figure 3.28. The different delays listed above are visible, limited by the vertical lines and labelled as (1) the set delay of $5.15 \mu\text{s}$, (2) the LED rise time of $0.1 \mu\text{s}$, (3) the drift time in the detection volume of $0.03 \mu\text{s}$, (4) the drift time in the GEM region of $0.03 \mu\text{s}$ and (5) some delay of unknown origin and the start of the first signals.

4. Measurements of ^{55}Fe Content in Activated Steel Samples

This chapter reports on measurements of the ^{55}Fe content in activated steel samples performed with the GEMPix. Handling of radioactive waste from accelerators and experiments at CERN is introduced in section 4.1. The measurement procedure, analysis and results are presented in sections 4.2 and 4.3 respectively. Section 4.4 draws conclusions and provides an outlook. This chapter was partially published in [103].

4.1. Introduction

At CERN and other facilities housing particle accelerators – including hospitals with particle accelerators for cancer treatment – material of the accelerator and the experiments in the proximity of the particle beam can be activated, meaning the production of radioactive isotopes in the material. When the material of the accelerator or the experiment is no longer used, it becomes radioactive waste and must be treated according to the applicable legislation. As a first measure it is usually stored temporarily – at CERN, this is on-site in the former Intersecting Storage Rings (ISR) – to allow for characterisation, sorting and other treatment. After interim storage the waste must be sent to a national repository or proven to have an activity below certain limits and released by a well-defined clearance procedure⁽¹⁾. Sometimes waste can even be reused at CERN as for the LHC beam dumps [107, p. 130].

4.1.1. Radioactive Waste at CERN

The radioactive waste at CERN has the following characteristics [108]:

⁽¹⁾The International Atomic Energy Agency (IAEA) defines clearance as ‘the removal of radioactive materials or radioactive objects within authorised practices from any further regulatory control by the regulatory body’ [106, p. 3].

- The vast majority of radioactive waste at CERN is a candidate for clearance or disposal as very-low-level activity / très faible activité (TFA) waste. Only a small fraction of waste is classified as low-level or intermediate activity waste, for example beam dumps and targets, where the beam interacts directly with the material. No high level activity waste is produced at CERN.
- Only a limited amount of activated or contaminated liquids is produced, typically the waste is solid.
- There are various possible activation channels due to different particle types and energies at CERN, resulting in a wide range of possibly produced radionuclides. A typical radionuclide inventory can be found in [108], with ^{55}Fe being one of the important nuclei for example in steel.
- Only radionuclides with a short half-life, defined as less than about 30 years [109, p. 7], are present.
- The local distribution of the activity can be very inhomogeneous for large components such as the radiofrequency (RF) cavities of the former Large Electron-Positron Collider (LEP).

Radiological characterisation of the waste is necessary since it is required before releasing it as conventional waste or before acceptance by national repositories. In agreement with recommendations by the IAEA [110, pp. 20-21], the radionuclides are categorised at CERN according to the possibility to measure them [111]:

- Easy-to-Measure (ETM) nuclides: for example γ -emitting nuclides that can be measured non-destructively by gamma spectrometry such as ^{60}Co and ^{22}Na .
- Difficult-to-Measure (DTM) nuclides: nuclides which cannot be measured non-destructively but can be measured by methods such as radiochemical analysis. Examples are ^3H , ^{55}Fe , ^{63}Ni .

A possibility to quantify the DTM nuclides is the scaling factor method ([112], [113]): a relation between a DTM and a Key Nuclide (KN) is established by measurements and simulations. Then the specific activity of the DTM nuclide is determined by measuring the specific activity of the KN and applying the scaling factor.

France and Switzerland are CERN's two host states defining the legislation concerning the radioactive waste. CERN, the French Government and the Swiss Federal Council signed a Tripartite Agreement, stating that CERN uses radioactive waste disposal paths of the two countries on a fair share basis [114].

In France, the waste coming from an accelerator complex and related experiments is stored in long-term storage facilities according to its activity and the half-life

of the present radionuclides. The hazard factor Indice Radiologique d'Acceptation en Stockage (IRAS) was developed by the French National Agency for Radioactive Waste Management (ANDRA) to establish criteria for waste acceptability to repositories for TFA waste [115]. The IRAS is defined as [111]:

$$IRAS = \sum_i \frac{a_i}{AL_i} \quad (4.1)$$

where a_i is the specific activity in Bq/g and AL_i is the specific activity limit of the radionuclide i .

Contrary to France, a pathway for clearance of radioactive waste as conventional waste exists in Switzerland. Three criteria must be fulfilled concerning surface contamination, ambient dose equivalent rate and a limit on a quantity similar to the *IRAS* called summation rule (Swiss legislation: [116], for an overview see for example [117, pp. 44-47]). An elimination campaign usually not only consists of measurements but also involves simulations and calculations of the expected radionuclide inventory by using FLUKA and ActiWiz [118], respectively. The activation of the material is predicted using the information on the use of the material, for example as an RF cavity in LEP, and accounting for the decay during interim storage. In the current clearance procedure in Switzerland, the radionuclides contributing together to at least 90% of the summation rule (similar to equation 4.1) need to be declared.

A recent example of a clearance project at CERN where ^{55}Fe was one of the radionuclides contributing the most to the summation rule is the clearance of the cavities of LEP [119]: about 2000 m³ of space in the temporary storage at CERN was emptied and approximately 95 % of the material was declared as conventional waste. The above mentioned clearance criteria had to be applied, scaling factors for the calculation of the ^{55}Fe activity had to be determined and radiochemical analysis of an external company was used to ensure a good estimate of the ^{55}Fe content.

4.1.2. ^{55}Fe

^{55}Fe is a radioactive isotope of iron with a half-life of 2.7 years⁽²⁾. Apart from direct beam impact, spallation and neutron capture are the dominant production processes occurring at CERN accelerators. In the case of LEP, photonuclear reactions (γ, n) play an important role as well. Therefore the ^{55}Fe production in iron is mainly possible through the $^{54}\text{Fe}(n, \gamma)^{55}\text{Fe}$ and $^{56}\text{Fe}(n, 2n)^{55}\text{Fe}$ reactions and – in case of LEP – via the $^{56}\text{Fe}(\gamma, n)^{55}\text{Fe}$ reaction. ^{56}Fe and ^{54}Fe are the natural isotopes of iron with occurrence of 91% and 5% respectively. Production channels starting from

⁽²⁾All numbers related to the decay of ^{55}Fe in this section are from [120, pp. 5-9].

other elements like Chromium or Manganese are possible but typically negligible since these elements only appear as traces in steel.

^{55}Fe decays by electron capture to ^{55}Mn leaving an electron level vacant. This vacancy is filled by an electron from a higher level under emission of Auger electrons or X-rays. The most dominant X-ray lines are the K_α -lines at 5.9 keV with about 25 X-rays per 100 decays. The K_β -lines at 6.5 keV happen about three times per 100 decays. Figure 4.1 shows the decay scheme. Because of the very low X-ray energy and therefore the strong self-attenuation in material it is a DTM nuclide. It is present mainly in radioactive steel waste and therefore very common in radioactive waste at CERN. The Swiss clearance limit at the time the analysis presented in this chapter was performed was 30 Bq/g [121]. However, on 1st January 2018 it was increased to 1 kBq/g [116]. The activity of ^{55}Fe is currently assessed at CERN using the radiochemical technique which is performed by an external company like AMEC (United Kingdom). Therefore samples need to be shipped for the analysis which takes typically about two months in total for a few samples. For the analysis the sample is dissolved and its activity is determined by a liquid scintillator. A detection limit for ^{55}Fe in metals of about 0.3 Bq/g to 0.5 Bq/g is reached by AMEC company.

The following sections report on measurements performed with the GEMPix to investigate whether this could be a faster in-house method sensitive to the Swiss clearance limit to determine the ^{55}Fe content in activated samples of radioactive metal waste.

4.2. Measurements of ^{55}Fe with the GEMPix

4.2.1. Sample Thickness

Since the energy of the ^{55}Fe X-rays is very low, many photons are absorbed in the (radioactive) material itself. Other radionuclides such as ^{44}Ti , ^{54}Mn and ^{60}Co are typically present together with ^{55}Fe but emit photons with higher energies and therefore longer attenuation lengths: for example the attenuation length in iron for 6 keV photons of ^{55}Fe is 15 μm while for 1.25 MeV photons of ^{60}Co it is 2.34 cm⁽³⁾. In order to increase the signal-to-background ratio, the sample thickness is reduced.

⁽³⁾These values are calculated using the mass attenuation coefficients and the density of iron provided in the NIST online database [94], first published in [95]. Only values at certain energies are available and therefore values for 6 keV and 1.25 MeV are used for ^{55}Fe (5.9 keV X-rays) and ^{60}Co (1.17 MeV and 1.33 MeV photons) respectively.

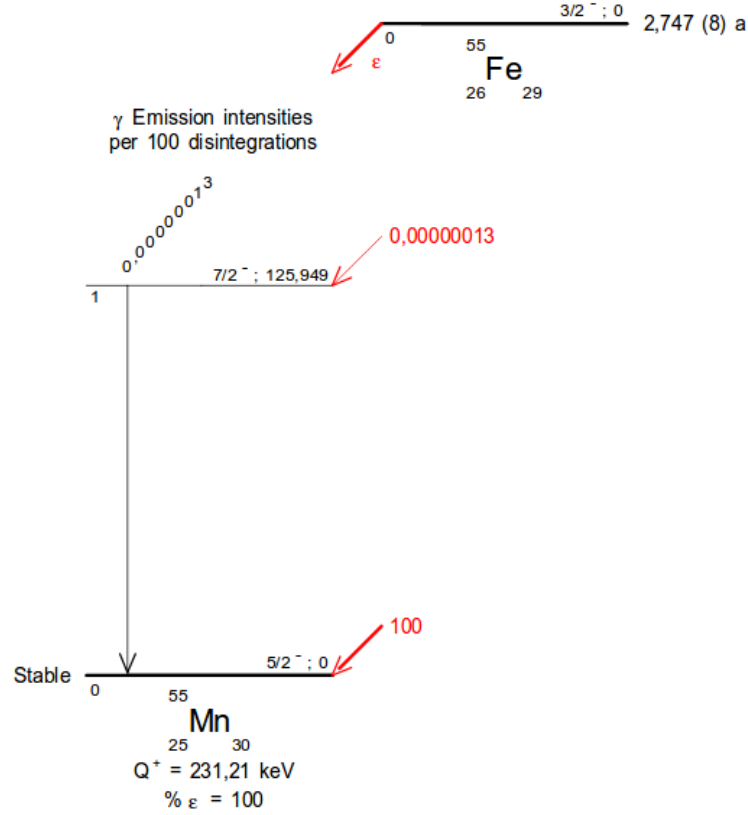


Figure 4.1: ^{55}Fe decays by electron capture to the stable ^{55}Mn [120, p. 9].

This is motivated by the fact that the ratio of photons escaping from the sample to photons emitted in the sample depends on the sample thickness:

$$\frac{N_{\text{photons,escaped}}}{N_{\text{photons,emitted}}} = \int_{0\text{ cm}}^t \frac{1}{t} \exp\left(-\frac{x}{\lambda}\right) dx = \frac{\lambda}{t} \left[1 - \exp\left(-\frac{t}{\lambda}\right)\right] \quad (4.2)$$

where t is the sample thickness, x the depth position in the sample, λ the attenuation length and N the number of photons. Figure 4.2 shows the calculated ratio in dependence of the sample thickness for ^{55}Fe . Two simplifying assumptions need to be made for this formula: the radionuclides are equally distributed in the sample and the problem is one dimensional in the sense that geometrical effects are neglected.

For a typical sample thickness reduction the percentage of ^{55}Fe X-rays escaping from the sample will increase drastically while the one of ^{60}Co gammas will increase only mildly, which in total improves the signal-to-background ratio. For instance, if the sample thickness is reduced from 1 cm to 100 μm , the escape probability for 6 keV X-rays increases by two orders of magnitude from 0.15% to 15% while the escape probability of 1.25 MeV photons only increases mildly from 81% to almost 100%.

Of course, the probability that ^{60}Co photons produce a signal in the energy regime of interest for ^{55}Fe is rather low⁽⁴⁾. Nevertheless, it is advantageous to start from a clean signal in the first place, considering also that the ^{60}Co content in the sample could be much larger than the ^{55}Fe content. Therefore the samples for this project are ground and the samples have a uniform sample thickness.

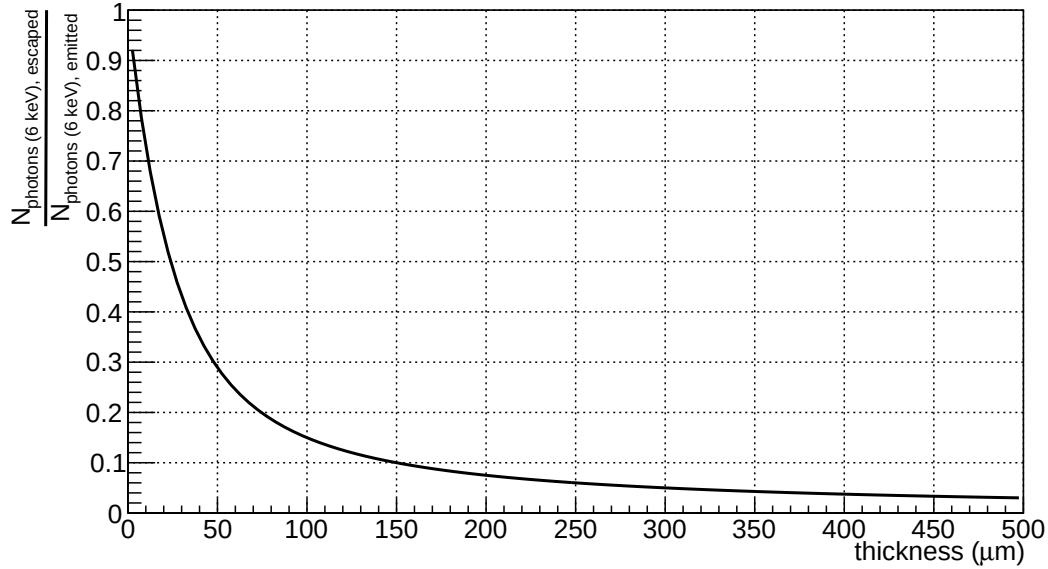


Figure 4.2: Escape probability of 6 keV photons in iron [103]. The escape probability of 1.25 MeV photons (^{60}Co) is almost constant within the shown thickness range – it is always larger than 98 %.

4.2.2. Sample Preparation

As during a usual clearance campaign, samples of the waste to be examined are selected and cut from the metallic waste⁽⁵⁾. A drill is then used to produce about 1 g of powder per sample. The powder is filtered with a mesh of 0.5 mm hole diameter and filled in a small plastic box. A double-sided piece of scotch – attached to the bottom of the plastic box before placing the powder – ensures good adhesion of the powder and allows to remove extra powder, after the powder was gently treated with

⁽⁴⁾High energy photons like the ones from ^{60}Co are likely to undergo a Compton effect and the resulting electron may leave tracks of ‘blobs’ in the GEMPix resembling the ones produced by ^{55}Fe X-rays.

⁽⁵⁾Sample preparation and many of the sample measurements with the GEMPix are performed by colleagues from the CERN HSE-RP-SP section.

a parallel punch for better adhesion. Therefore a rather homogeneous thickness of about $100\text{ }\mu\text{m}$ is achieved. Figure 4.3 shows a picture of a sample box with dimensions $4 \times 4 \times 1\text{ cm}^3$.



Figure 4.3: The sample powder is attached to the bottom of a plastic box [103]. The box can be closed for safer storage and opened for measurements.

4.2.3. Experimental Set-up and Measurement Procedure

The GEMPix is placed inside a lead shielding to reduce background from ambient gamma rays. Figure 4.4 shows the set-up. The usual detection gas $\text{Ar}:\text{CO}_2:\text{CF}_4$ (45:15:40) is flushed through the GEMPix at 3l/h at about 1 bar. A gain of 1240 V is used. Four measurements per sample are necessary to determine the ^{55}Fe content:

1. Calibration measurement with an ^{55}Fe source.
2. Sample measurement.
3. Calibration measurement with an ^{55}Fe source.
4. Sample gamma background measurement.

The calibration measurements are used to define the counting range in energy for the sample and sample background measurements, i.e. to compensate for example possible changes in the detector due to temperature and pressure as these measurements are performed before the described corrections (section 3.4.5) are developed. The sample gamma background measurement is performed with a thin aluminium sheet between the sample and the detector. This sheet is about $100\text{ }\mu\text{m}$ thin, corresponding to about three attenuation lengths of ^{55}Fe photons and therefore strongly suppressing the ^{55}Fe signal while not affecting the high energy photons⁽⁶⁾. The nominal Pixelman settings for all types of measurements are: a frame length of 1s; an

⁽⁶⁾Only 4.5% of ^{55}Fe photons compared to 99.9% of ^{60}Co photons pass through $100\text{ }\mu\text{m}$ of aluminium. These values are calculated using the mass attenuation coefficients and the density of iron provided in the NIST online database [94], first published in [95]. Only values at certain

energy threshold of about 100 eV; TOT mode; a Timepix clock of 48 MHz. The sample and the sample gamma background measurements last about 2 h each – 7200 frames are acquired – while the calibration measurements last 10 min (600 frames) each.

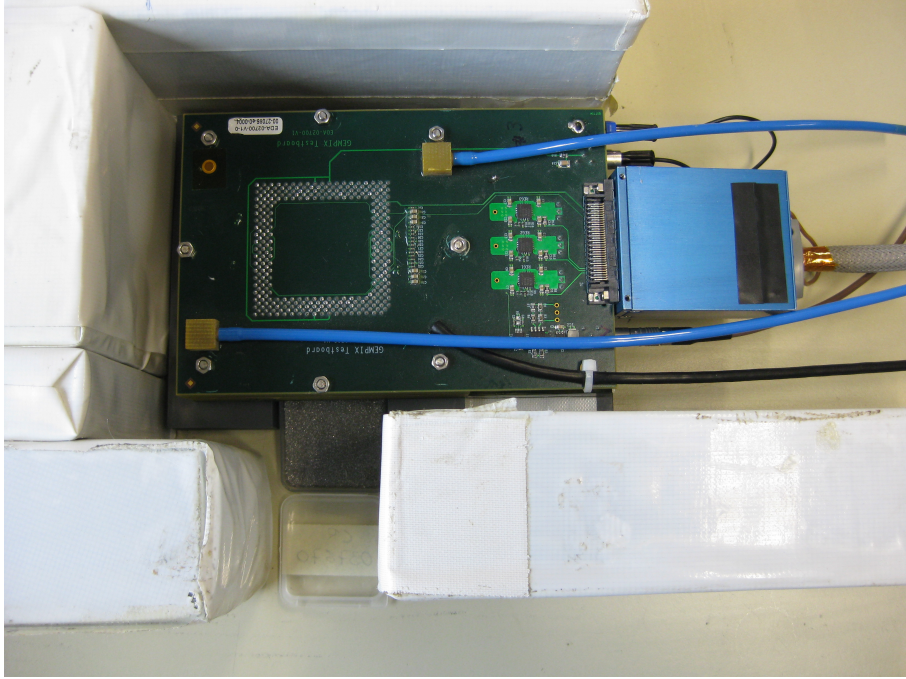


Figure 4.4: A sample in the small plastic container is ready to be moved below the GEMPix entrance window. The set-up is surrounded by lead bricks (wrapped in white scotch) for shielding; the top layer was removed for this picture.

4.3. Data Analysis and Results

4.3.1. Data Analysis

The main analysis is performed offline. However, some online monitoring is performed: each event is displayed in the standard Pixelman software and – thanks to a custom script in the Python plug-in – the values of the main parameters and their time evolution are shown. A cluster analysis reduces the amount of data to be saved:

energies are available and therefore values for 6 keV and 1.25 MeV are used for ^{55}Fe (5.9 keV X-rays) and ^{60}Co (1.17 MeV and 1.33 MeV photons) respectively.

only 19 parameters per cluster are saved instead of the measured TOT counts of each pixel in each frame. The saved parameters include the frame start time, the number of clusters in the frame, the cluster type, the cluster size, the cluster position and the TOT counts of the cluster⁽⁷⁾. Only clusters of type ‘heavy blob’ are used in the analysis, which are the clusters typically produced by low energy X-rays and which fulfil the following conditions [122]:

- Minimum ratio of inner to border pixels: 0.5.
- Maximum deviation from perfect circle, i.e. ratio of the diameter calculated from cluster size and the maximum distance within the cluster: 1.2.

Clusters that are close to the edge of a Timepix chip are discarded as they may not be fully contained in the readout and as some non-uniformities of the electric field at the edges of the quad Timepix have been observed. The centre of the cluster c must be within $25 < c < 246$ or $266 < c < 487$, where the numbers state the pixel number in x or y from 0 to 511.

The energy spectrum of the remaining clusters is then analysed. It is expected to have two main peaks, the photopeak and the Argon escape/fluorescence peak: a 5.9 keV photon of ^{55}Fe will most likely undergo a photoelectric effect emitting a photoelectron from the K-shell of Argon (binding energy: 3.2 keV) [22, p. 242]. The dominant process to fill the vacancy in the K-shell is the emission of Auger electrons. Only in about 15% a characteristic X-ray of 3 keV and an Auger electron of 0.2 keV are emitted. The events contribute to the photopeak if the total energy is detected. If the X-ray escapes the detection volume, only the remaining energy of 2.9 keV is detected (so-called Argon escape peak). If the X-ray is detected elsewhere in the volume, it contributes to the Argon fluorescence peak of 3 keV which cannot be resolved from the escape peak. Figure 4.5 shows a spectrum of a source measurement and figure 4.6 shows a sample measurement. The source measurement is used to define a counting range for the sample measurement by fitting a Gaussian function to the 5.9 keV peak: the range for the sample is defined as $\mu \pm 2\sigma$.

4.3.2. Samples, Radiochemical and GEMPix Results

A total of 45⁽⁸⁾ activated steel samples are selected for the GEMPix measurements. The samples are collected during elimination campaigns of the metallic waste

⁽⁷⁾In the appendix (section A.4) there is an explanation of all saved parameters.

⁽⁸⁾Originally, 55 samples were selected including ten samples from other waste packages or activation experiments. The ten other samples were sent to other laboratories for radiochemical analysis. However, discrepancies were noticed when the radiochemical analysis for some sample was repeated. The origin of the discrepancies could not be figured out but in order to achieve

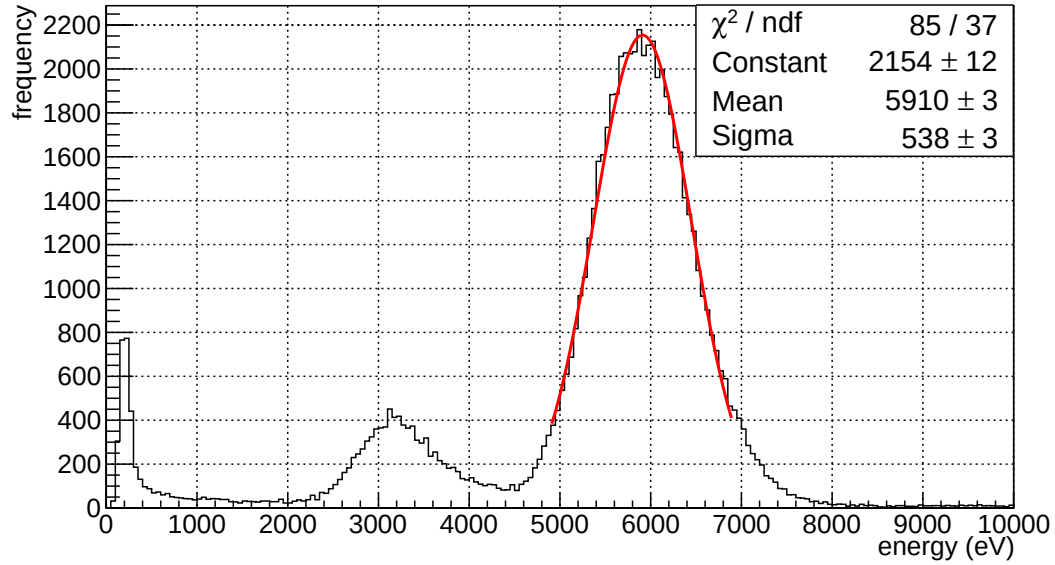


Figure 4.5: The energy spectrum of a measurement with an ^{55}Fe source [103]. Here, events within (5910 ± 1076) eV would be counted in the sample and background measurements. The peak around 3 keV is due to the Argon fluorescence and escape peaks. Peaks deviate slightly from Gaussian shape probably due to small gain variations in different regions of the GEMPix (see section 3.4.2).

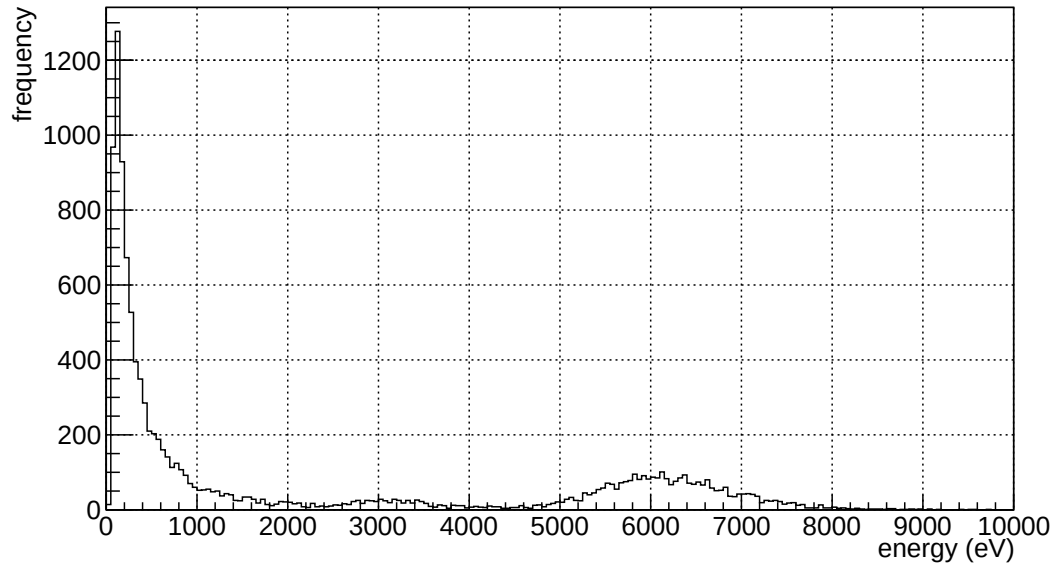


Figure 4.6: The energy spectrum of a sample measurement [103].

(SHERPA) and during the studies for the disposal of the LEP superconducting RF cavities (LEP). Each collected sample is divided in two pieces: the first is sent to an external company (AMEC, [123]) for radiochemical analysis, the second to the CERN workshop to be ground and the powder to be measured with the GEMPix (as described in section 4.2.2).

Table 4.1 shows both, the results obtained by the radiochemical analysis as well as those obtained with the GEMPix. The table provides for each sample a sample number, the identification code in the Traceability of Radioactive Equipment at CERN (TREC) database [124], the sample origin (SHERPA or LEP), the measurement duration and the results. A decay correction is applied to the radiochemical results in order to take into account the decay of ^{55}Fe due to the time difference between the GEMPix measurements and the radiochemical analysis. Most of the GEMPix measurements last 7200 s. The column ‘GEMPix (counts per 1000 s)’ shows the net results of the measurements: the sample background measurement is subtracted from the sample measurement. Results are normalised to a duration of 1000 s. For several samples, the background is not measured, and an estimated background of 50 counts in 7200 s is stated instead⁽⁹⁾. This is based on the fact that the lowest measured background in 7200 s is 42 counts, which implies that the true mean value of the lowest background is somewhat larger. Furthermore, the estimation of 50 counts leads to an offset in the fit of the calibration curve (figure 4.7) that is compatible with zero. However, due to the background estimation and expected statistical fluctuations, some GEMPix results (background subtracted counts and specific activity) are negative. Uncertainties are stated at 68% confidence level. For the GEMPix analysis, only the ‘counting uncertainty’⁽¹⁰⁾ is taken into account. The other columns of table 4.1 are discussed in the next sections.

a consistent set of samples and measurement procedure it was decided to discard the extra ten samples.

⁽⁹⁾Table A.3 in section A.5 of the appendix shows the results of the sample measurement and of the sample background measurement, or if this estimated background is used.

⁽¹⁰⁾Sigma is equal to the square root of the number of events.

Table 4.1.: Results of all samples measured to determine the ^{55}Fe content.

no.	TREC /ID	Sample origin	Duration (s)	Radio-chemical (Bq/g)	GEMPix (counts per 1000s)	GEMPix (Bq/g)	Radio-chemical - GEMPix (Bq/g)	difference / sum of uncertainties
1	CR-028446	SHERPA	7200	0.58 ± 0.17	-0.97 ± 1.34	-1.60 ± 2.20	2.2 ± 2.4	0.9
2	CR-028418	SHERPA	7200	0.67 ± 0.20	-2.36 ± 1.27	-3.88 ± 2.08	4.6 ± 2.3	2.0
3	CR-028557	SHERPA	7200	1.38 ± 0.23	-1.39 ± 1.32	-2.28 ± 2.17	3.7 ± 2.4	1.5
4	CR-037144	SHERPA	7200	1.49 ± 0.26	-2.92 ± 1.23	-4.80 ± 2.03	6.3 ± 2.3	2.7
5	CR-037138	SHERPA	7200	0.64 ± 0.23	-1.11 ± 1.33	-1.83 ± 2.19	2.5 ± 2.4	1.0
6	CR-028426	SHERPA	7200	1.38 ± 0.22	-0.56 ± 1.36	-0.91 ± 2.24	2.3 ± 2.5	0.9
7	CR-037654	LEP	50400	4.64 ± 0.35	1.67 ± 0.57	2.74 ± 0.94	1.9 ± 1.3	1.5
8	CR-028406	SHERPA	7200	3.93 ± 0.34	-0.28 ± 1.37	-0.46 ± 2.26	4.4 ± 2.6	1.7
9	CR-037147	SHERPA	7200	1.34 ± 0.23	0.14 ± 1.40	0.23 ± 2.30	1.1 ± 2.5	0.4
10	CR-028553	SHERPA	7200	1.40 ± 0.22	-0.42 ± 1.37	-0.69 ± 2.25	2.1 ± 2.5	0.8
11	CR-036728	SHERPA	7200	1.71 ± 0.26	-1.25 ± 1.32	-2.06 ± 2.18	3.8 ± 2.4	1.5
12	CR-028432	SHERPA	7200	6.17 ± 0.50	0.28 ± 1.40	0.46 ± 2.31	5.7 ± 2.8	2.0
13	CR-037148	SHERPA	7200	0.97 ± 0.23	0.69 ± 1.42	1.14 ± 2.34	-0.2 ± 2.6	-0.1
14	CR-028384	SHERPA	7200	1.15 ± 0.21	1.11 ± 1.44	1.83 ± 2.37	-0.7 ± 2.6	-0.3
15	CR-037140	SHERPA	7200	2.07 ± 0.25	1.81 ± 1.48	2.97 ± 2.43	-0.9 ± 2.7	-0.3
16	CR-028382	SHERPA	7200	2.12 ± 0.26	1.11 ± 1.44	1.83 ± 2.37	0.3 ± 2.6	0.1
17	CR-028430	SHERPA	7200	0.88 ± 0.19	2.08 ± 1.49	3.43 ± 2.45	-2.6 ± 2.6	-1.0
18	CR-028354	SHERPA	7200	16.0 ± 1.1	2.92 ± 1.53	4.80 ± 2.52	11 ± 4	3.1
19	CR-028448	SHERPA	7200	0.43 ± 0.18	2.50 ± 1.51	4.11 ± 2.48	-3.7 ± 2.7	-1.4
20	CR-037146	SHERPA	7200	1.25 ± 0.22	4.72 ± 1.61	7.77 ± 2.65	-6.5 ± 2.9	-2.3
21	CR-028400	SHERPA	7200	3.45 ± 0.34	6.25 ± 1.67	10.3 ± 2.8	-6.8 ± 3.1	-2.2
22	CR-028428	SHERPA	7200	1.83 ± 0.24	2.92 ± 1.53	4.80 ± 2.52	-3.0 ± 2.8	-1.1
23	CR-028394	SHERPA	7200	0.40 ± 0.18	2.36 ± 1.50	3.88 ± 2.47	-3.5 ± 2.7	-1.3

Table 4.1.: Results of all samples measured to determine the ^{55}Fe content (continued).

no.	TREC /ID	Sample origin	Duration (s)	Radio-chemical (Bq/g)	GEMPix (counts per 1000s)	GEMPix (Bq/g)	Radio-chemical - GEMPix (Bq/g)	difference / sum of uncertainties
24	CR-036727	SHERPA	7200	0.88 ± 0.19	3.19 ± 1.54	5.25 ± 2.54	-4.4 ± 2.7	-1.6
25	CR-028555	SHERPA	7200	1.45 ± 0.23	3.19 ± 1.54	5.25 ± 2.54	-3.8 ± 2.8	-1.4
26	CR-036725	SHERPA	7200	2.11 ± 0.29	4.03 ± 1.58	6.63 ± 2.60	-4.5 ± 2.9	-1.6
27	CR-028388	SHERPA	7200	2.17 ± 0.25	4.44 ± 1.60	7.31 ± 2.63	-5.1 ± 2.9	-1.8
28	CR-028422	SHERPA	7200	27.1 ± 1.7	10.8 ± 1.9	17.8 ± 3.1	9.3 ± 4.8	1.9
29	CR-028392	SHERPA	7200	14.2 ± 1.0	11.4 ± 1.9	18.7 ± 3.1	-4.6 ± 4.1	-1.1
30	CR-028390	SHERPA	7200	7.60 ± 0.56	22.8 ± 3.9	37.5 ± 6.3	-30 ± 7	-4.4
31	CR-028412	SHERPA	5980	27.8 ± 1.8	25.3 ± 2.6	41.7 ± 4.4	-14 ± 6	-2.2
32	CR-028444	SHERPA	6221	52.0 ± 3.3	24.0 ± 2.4	39.4 ± 4.0	13 ± 7	1.7
33	CR-028434	SHERPA	7200	50.9 ± 3.2	26.3 ± 2.3	43.2 ± 4.0	7.6 ± 7.1	1.1
34	CR-028386	SHERPA	7200	54.9 ± 3.5	36.5 ± 2.7	60.1 ± 4.6	-5.2 ± 8.0	-0.6
35	CR-028374	SHERPA	7200	35.7 ± 2.3	60.0 ± 3.7	98.7 ± 6.5	-63 ± 9	-7.1
36	CR-028408	SHERPA	7200	66.2 ± 4.1	56.0 ± 3.2	92.1 ± 5.6	-26 ± 10	-2.6
37	CR-037656	LEP	7200	214 ± 13	147 ± 5	242 ± 10	-28 ± 23	-1.2
38	CR-037450	SHERPA	7200	104 ± 7	70.3 ± 3.6	116 ± 6	-12 ± 13	-0.9
39	CR-037653	LEP	7200	125 ± 8	69.7 ± 3.4	115 ± 6	10 ± 14	0.7
40	CR-028424	SHERPA	7200	142 ± 9	78.3 ± 3.7	129 ± 7	13 ± 15	0.8
41	CR-028410	SHERPA	7200	115 ± 7	63.6 ± 3.3	105 ± 6	11 ± 13	0.8
42	CR-028376	SHERPA	7200	223 ± 14	119 ± 5	196 ± 9	26 ± 23	1.1
43	CR-028414	SHERPA	5709	222 ± 14	135 ± 6	222 ± 11	-0.1 ± 25	0.0
44	CR-037657	LEP	7200	572 ± 35	256 ± 6	420 ± 14	151 ± 49	3.1
45	CR-037655	LEP	7200	1145 ± 71.0	686 ± 10	1128 ± 31	16 ± 102	0.2

4.3.3. Calibration of the GEMPix

The GEMPix counts per second are plotted against the corresponding radiochemical results in order to obtain the calibration factor for the GEMPix (figure 4.7). The bad quality of the fit ($\chi^2/\text{ndf}=272/43$) is explained by an underestimation of the uncertainties on the GEMPix counts, since only the ‘counting uncertainty’ is considered, as discussed better in the next section. The calibration factor c is calculated using the slope of the fit function while neglecting the offset only relevant for very small activities:

$$c = \frac{1}{\text{slope}} = \frac{1}{(6.078 \pm 0.140) \cdot 10^{-4} \frac{\text{cps}}{\text{Bq/g}}} = 1645 \pm 38 \frac{\text{Bq/g}}{\text{cps}}. \quad (4.3)$$

The results of the GEMPix measurements after calibration in Bq/g and their comparison with the radiochemical results are also included in table 4.1. Negative specific activity values are due to negative net counts as explained above. Operationally, only upper limits for the specific activity would be set for these samples.

Figure 4.8 shows the distribution of the difference in units of the sum of the uncertainties of the two methods (the pull distribution). The values for each measurement are shown in the last column of table 4.1. The uncertainties of the two methods are added linearly to obtain the uncertainty on the difference⁽¹¹⁾. A Gaussian distribution with a mean of zero and a sigma of one is expected if the uncertainties are properly modelled. The fact that the fitted sigma is larger than one, suggests that the uncertainties are underestimated. This is believed to be the case because the only uncertainty assigned to the GEMPix results is the ‘counting uncertainty’.

4.3.4. Sensitivity of the Technique, Detection Limit, Confidence Levels and Uncertainties

In this section, a confidence level (C.L.) of 95% is chosen for all calculations. Note that uncertainties in table 4.1 are given on a 68% C.L. As an example, the sensitivity to a 30 Bq/g limit is calculated as this value was the current Swiss clearance limit for ^{55}Fe at the time the analysis was performed. Note that only one set of samples to develop the calibration and to check the sensitivity is used. Therefore, this analysis is only a proof-of-principle and a check with an independent sample set will be clearly necessary to judge the accuracy and reliability of the GEMPix measurements.

⁽¹¹⁾The stated uncertainty for the radiochemical analysis is defined differently than the uncertainty on the GEMPix results; i.e. it does not only include the ‘counting uncertainty’. In a conservative approach the uncertainties are added linearly.

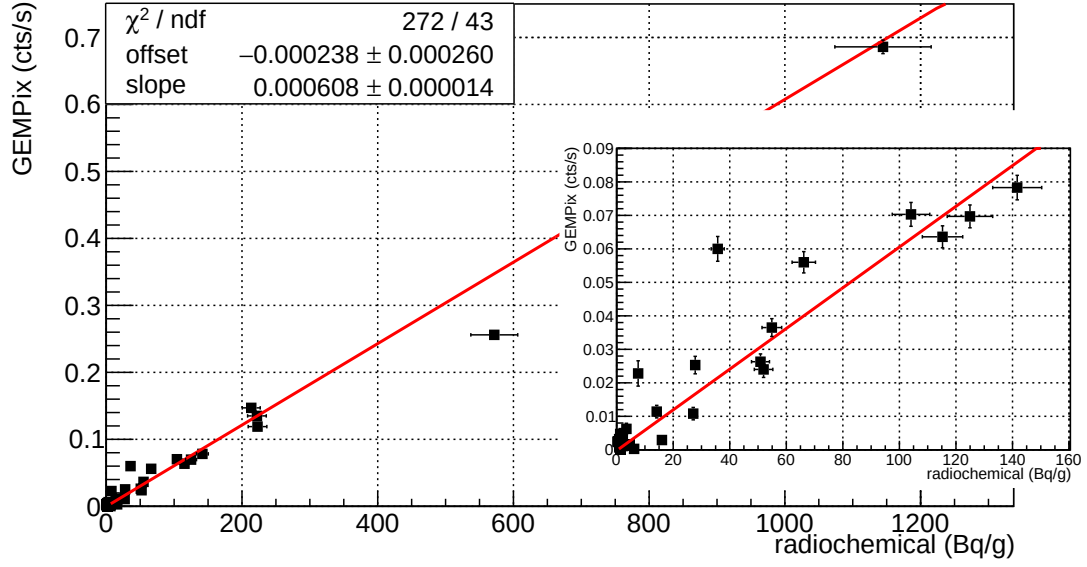


Figure 4.7: Calibration of GEMPix background subtracted counts against results of the radiochemical analysis. Inlet shows zoom to small specific activities as there are the most measurements. Similar figure in [103].

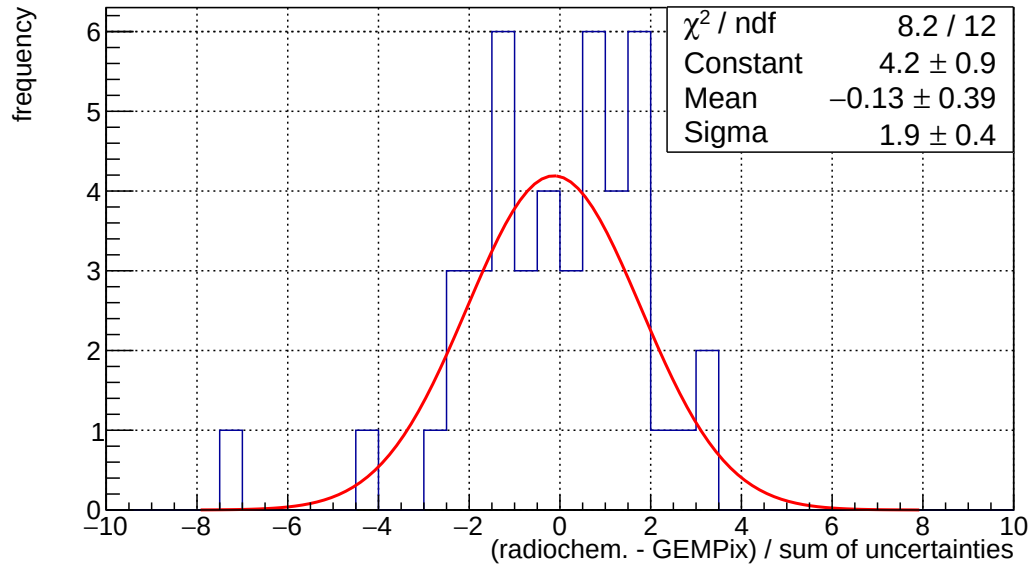


Figure 4.8: Difference of radiochemical and GEMPix measurements in units of the combined uncertainties [103].

The measured background is not independent of the sample itself since there is a non-negligible contribution from other radionuclides present in the sample. Figure 4.9 shows the distribution of the background measured for 16 out of 45 samples.

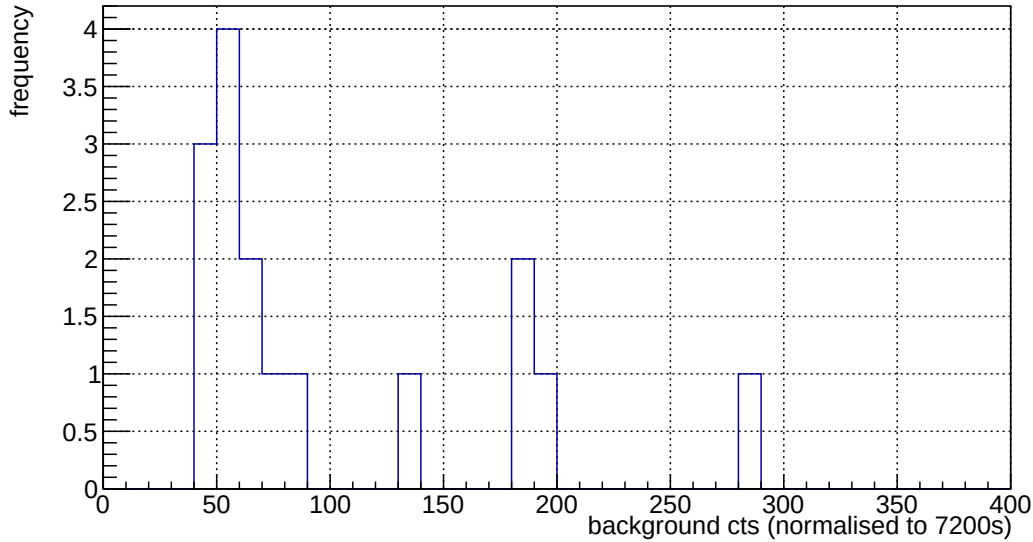


Figure 4.9: Sample background of the GEMPix measured for 16 samples [103].

Detection limits of the technique are calculated depending on the background using Poisson statistical methods. The 95% C.L. single-sided upper limits for each number of background counts is calculated according to [125]: for count numbers, n , smaller than 51 the upper limit is taken directly from a table provided in the reference, for larger count numbers the upper limit, $u.l.$ is approximated by a formula given in the reference:

$$u.l. = (n + 1) \left(1 - \frac{1}{9(n + 1)} + \frac{1.65}{3\sqrt{n + 1}} \right)^3. \quad (4.4)$$

Figure 4.10 shows the resulting upper limits for each number of background counts. These upper limits are interpreted as the detection limit above which ^{55}Fe content is detected. For example, if 100 background counts and 110 (150) total counts are measured, the result is (is not) compatible with the background-only hypothesis at 95% C.L. Figure 4.11 shows the detection limit after background subtraction as a specific activity for each number of background counts, using the calibration factor calculated in section 4.3.3. The detection limit is well below 10 Bq/g for all background counts of the 45 samples. Note that this is only the statistical detection limit. From the results in table 4.1 it is evident that this detection limit is not reached in practice due to larger systematic uncertainties.

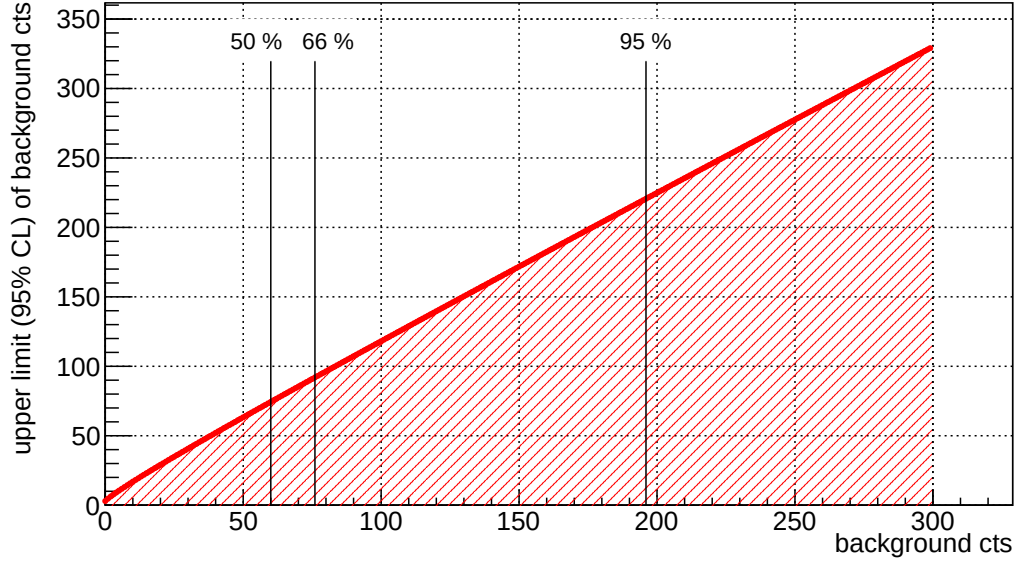


Figure 4.10: The upper limits are calculated for each number of background counts (red points) [103]. Above this limit, the detector is sensitive to ^{55}Fe . Below this limit, in the shaded area, background only cannot be excluded. The vertical lines show the maximum background counts for a stated fraction of the measured samples (numbers on top of lines).

Figure 4.12 compares the GEMPix results with the calculated detection limit. Also, the total number of counts for a sample with a specific activity of 30 Bq/g is calculated for each number of background counts. For this, the specific activity of 30 Bq/g is converted to number of counts using the calibration factor and the number of background counts is added. The 95% C.L. single-sided lower limit for the clearance limit plus background is calculated using the tables provided in [125], equation 4.4 for the upper limit for more than 50 counts, and the following equation 4.5 for the lower limit, $l.l.$, in case of more than 50 counts, n .

$$l.l. = n \left(1 - \frac{1}{9n} - \frac{1.65}{3\sqrt{n}} \right)^3 \quad (4.5)$$

Thus, if a data point is:

- Below detection limit, the total number of counts is compatible with the background-only hypothesis.
- Above detection limit, the background-only hypothesis is ruled out and we infer that there is some ^{55}Fe content in the sample.

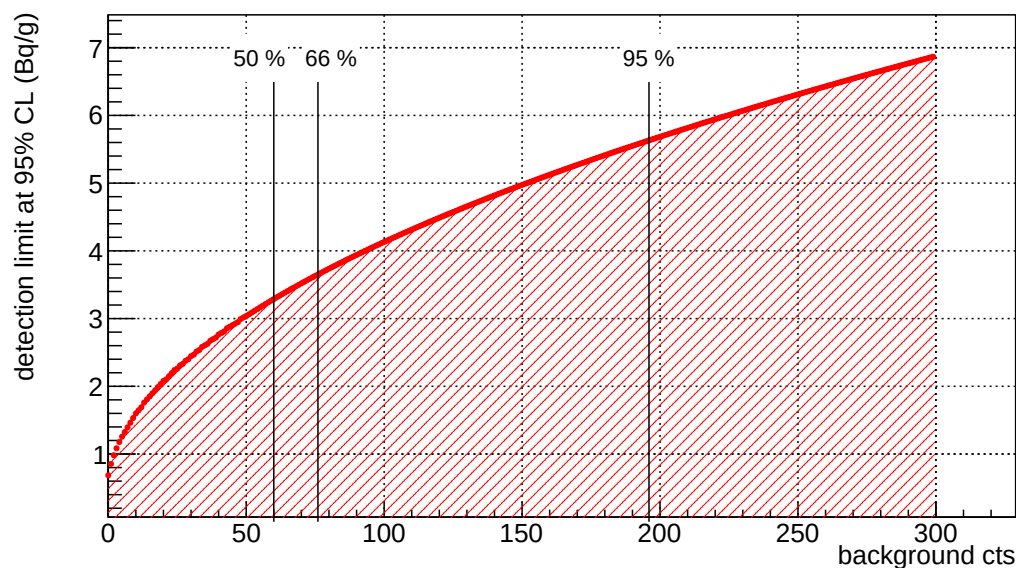


Figure 4.11: The upper limits shown in figure 4.10 are background subtracted and then converted to specific activity using the calibration factor [103]. Above the limit, the detector is sensitive to ^{55}Fe . Below this, in the shaded area, background only cannot be excluded. The vertical lines show the maximum background counts for a stated fraction of the measured samples (numbers on top of lines).

- Below the lower limit of the clearance limit, the specific activity of the sample is less than 30 Bq/g.
- Above the lower limit of the clearance limit, we cannot exclude a specific activity larger than 30 Bq/g.

All statements are at 95% C.L. Furthermore, figure 4.12 shows a comparison with radiochemical analysis with different marker styles and colours. If a data point is a:

- red upwards pointing triangle: the specific activity of the sample measured by radiochemical analysis is larger than 30 Bq/g minus its uncertainty at 95% C.L.
- green downwards pointing triangle, the specific activity of the sample measured by radiochemical analysis is smaller than 30 Bq/g minus its uncertainty at 95% C.L.

Results of the radiochemical analysis and of the GEMPix are inconsistent with respect to the clearance limit for two of the 45 samples: for sample no. 30 the GEM-

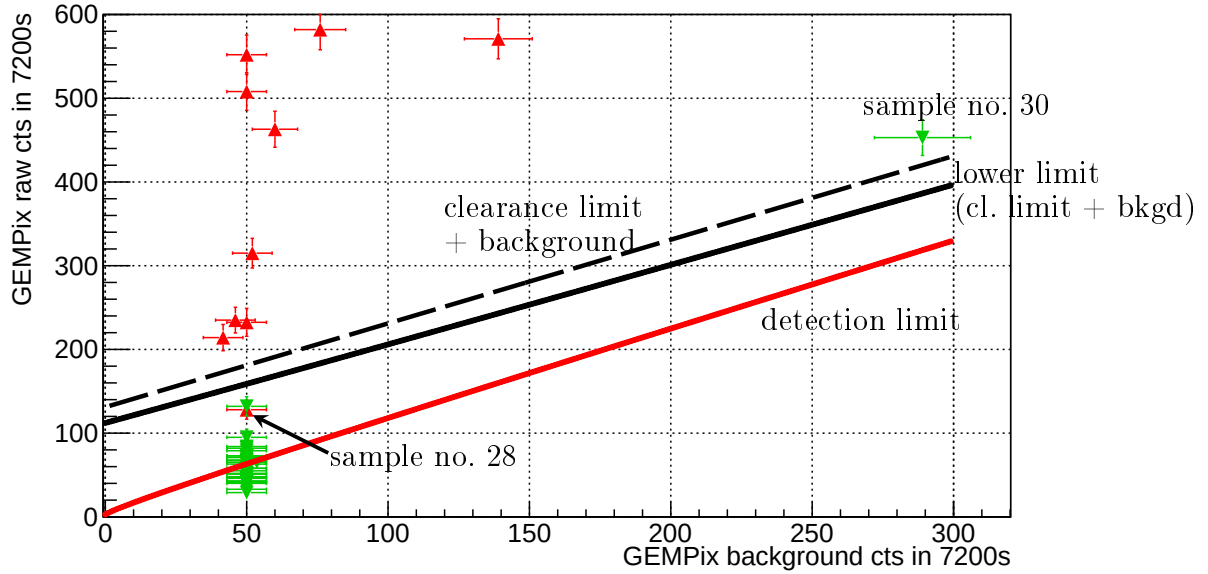


Figure 4.12: GEMPix raw versus background counts (data points) of the samples are compared with the detection limit (solid red line, compare figure 4.10) and the Swiss clearance limit of 30 Bq/g plus background (black dashed line) [103]. Solid black line shows 95% C.L. lower limit of the clearance limit plus background. Radiochemical analysis results are encoded for sample data points: red upwards (green downwards) pointing triangles denote specific activity plus uncertainty at 95% C.L. above (below) clearance limit. Some samples are out of range on the y-axis of this plot but they are well above the detection limit and all are correctly assigned to have a specific activity larger than 30 Bq/g.

Pix states a specific activity above 30 Bq/g while the radiochemical analysis states a specific activity below 30 Bq/g. The results for sample no. 28 show the inverted situation. Thus, sample no. 28 would be falsely declared to have a specific activity below the clearance limit. However, it is expected that a complete uncertainty investigation of the GEMPix would result in larger uncertainties. The probability to falsely state that a specific activity is below 30 Bq/g would be decreased. At the same time, a larger uncertainty on the GEMPix results will correspondingly reduce the sensitivity. This is less problematic for larger clearance limits since the majority of ^{55}Fe samples typically has a rather low specific activity. As of 2018, the new Swiss clearance limit is 1000 Bq/g.

The complete analysis presented in this section is limited by the fact that only statistical uncertainties on the counting are considered. An investigation of other

uncertainties is necessary before defining operational limits with respect to the Swiss clearance limit. Sources of other uncertainties include sample preparation, stability of the GEMPix and positioning of the samples below the GEMPix.

4.4. Conclusions and Outlook

A new method to measure the ^{55}Fe content in radioactive samples using the GEMPix is developed. A procedure to measure the background and the total counts of a sample is designed. In total, measurement of one sample takes approximately 4.5 h. Forty-five samples from CERN's radioactive waste are used to calibrate the detector. Measured counts are converted into specific activity using a calibration curve based on reference data from radiochemical analyses of the same samples.

Since the background is sample-dependent, the detection limit is also background-dependent and has been accounted for in the calculation of the detection limits. From the 45 samples analysed, good agreement is found between the radiochemical analysis and the present procedure. As an example, the sensitivity to 30 Bq/g, which was the Swiss clearance limit for ^{55}Fe before 2018, is investigated but only statistical uncertainties of the method are included. The method is potentially sensitive to the clearance limit. A complete uncertainty study is needed. This will most likely reduce the sensitivity of the method though this will be less important since the activity of most of the samples is small compared to the new Swiss clearance limit of 1 kBq/g. It can be investigated whether this method could be extended to other DTM radionuclides such as ^{63}Ni and ^{36}Cl with a clearance limit of 100 Bq/g and 1 Bq/g respectively.

The calibration to convert GEMPix counts into activity is essential for this technique and can be improved by the use of sources with a well-defined activity. Liquid sources that can be diluted until the wanted activity is reached could be used to develop the conversion based on measurements at different activities. Due to the increase of the clearance limit to 1 kBq/g, the contribution of ^{55}Fe to the summation rule for clearance at CERN decreased: the same activity of ^{55}Fe is now divided by a larger clearance limit. However, ^{55}Fe remains an important radionuclide to be characterised for final storage which is the main elimination path of the radioactive waste at CERN.

5. Measurements of the 3D Energy Deposition in Water for Hadron Therapy

This chapter reports measurements and simulations of the energy deposition in a water phantom for hadron therapy. Section 5.1 introduces radiation therapy, CNAO, the treatment planning and the necessary quality assurance, providing the basis before motivating this project in section 5.2. Results obtained with the CNAO water phantom (section 5.3) are the reason to develop the integrated system (section 5.4) which is well tested (section 5.5). The energy deposition in a water phantom is investigated in details by simulations (section 5.6) and compared to measurements performed at CNAO with the integrated system (section 5.7). The work conducted for this project is concluded and an outlook provided in section 5.8. This chapter was partially published in [126].

5.1. Background

5.1.1. Cancer

In 2018 there are an estimated 3.9 million new cases of cancer and 1.9 million deaths from cancer in Europe [127]. In Germany cancer was the second most cause of death in 2015: about 25% of all deaths were caused by cancer [128, p. 3]. Therefore, cancer treatment is one of the most important tasks of the health care system and research on cancer and on cancer treatment is a major topic. Different treatment methods exist today, with surgery, radiation therapy and chemotherapy being the most important ones. The type of treatment depends on the type of cancer and often a combination of two different treatment methods is applied [129].

5.1.2. Radiation Therapy and Hadron Therapy

Soon after the discovery of X-rays by Röntgen in 1895 [130] it was anticipated that radiation could be used to treat cancer [131]. About 50% of cancer patients in Europe have indications to receive radiation therapy [132]. Radiation therapy can be either applied by radioactive sources or by accelerated particles. The conventional accelerator based radiation therapy accelerates electrons which are typically converted to photons. These machines are commercially available, can be built very compact and fit into a single room in a hospital. Worldwide more than 11,000 linear accelerators (LINACs) and more than 2,000 radionuclide teletherapy units are available. In Germany more than 500 LINACs and 20 radionuclide units exist⁽¹⁾.

Another choice of particles for accelerator based radiation therapy are hadrons like protons and carbon ions. The clear inherent advantage of hadron therapy over conventional photon therapy is the energy deposition of the particles with increasing penetration depth: photons show an exponentially decreasing energy deposition after a quick build-up at the entrance. On the contrary, hadrons produce a Bragg Curve (see section 2.2.1) with a clear maximum at a certain penetration depth. The position of the maximum, the Bragg peak, can be adjusted by tuning the energy of the primary beam. Figure 5.1 compares the energy deposition of photons and hadrons (in this case protons) versus depth. The important quantity for the biological effect is not only the physical dose but also the so-called relative biological effectiveness (RBE). It is defined as the ratio of the absorbed dose of a test radiation (in this case protons or carbon ions) to the reference radiation (X-rays) producing the same biological effect [134, p. 77]. While protons show a similar relative biological effectiveness (RBE) as photons, carbon ions have an enhanced RBE in the Bragg peak [11], supporting the sparing of healthy tissue in the entrance channel. The best choice of treatment depends on the type of tumour. Hadron therapy is for example often a good choice for paediatric tumours since the dose absorbed in healthy tissue is minimised, avoiding long-term effects by radiation-induced secondary tumours which is most important when treating children [135].

The medical use of protons was first proposed by Wilson in 1946 [137] and first patients were treated in 1954 [11]. However, hadron therapy has seen an increase in application only after the first clinical set-up in the early 1990s [138, p. 8]. As of the end of 2016, more than 170,000 patients have received treatment [139]. In Germany currently 6 particle therapy centres are operational, most of them using only protons accelerated by a cyclotron. Only the Heidelberg Ion-Beam Therapy Center (HIT) and the Marburg Ion-Beam Therapy Center (MIT) provide also carbon ions and

⁽¹⁾All numbers are extracted from the ‘Directory of Radiotherapy Centres’ of the IAEA, which is available online [133].

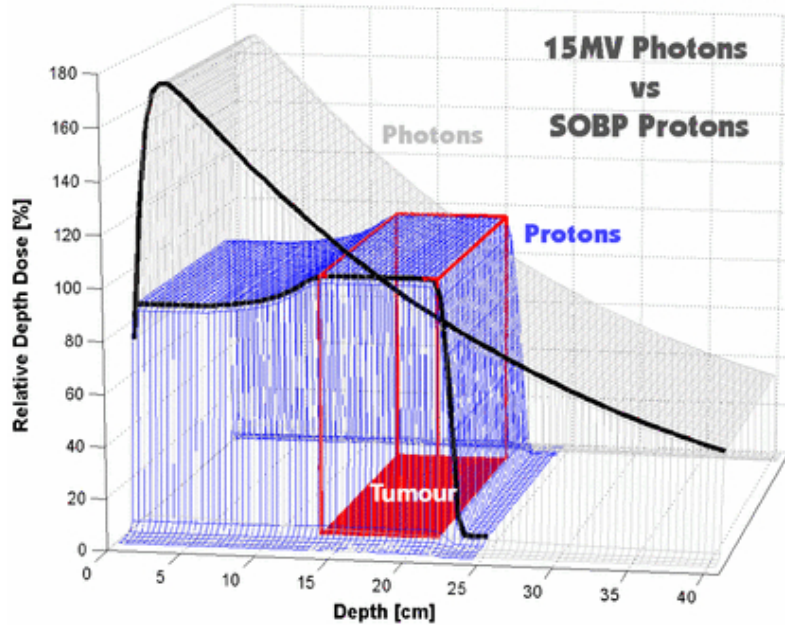


Figure 5.1: Comparison of photon and proton depth dose profile [136]. A Spread-Out Bragg Peak (SOBP) is a superposition of several Bragg curves of different energy, needed to extend the maximum dose over the tumour volume.

have a synchrotron. In Europe, in total 20 particle therapy centres are operational of which 16 have a cyclotron for proton acceleration and HIT, MIT, MedAustron (Austria) and CNAO (Italy) use a synchrotron that also provides carbon ions⁽²⁾.

5.1.3. Particle Acceleration: Synchrotron

A maximum penetration depth of about 25 cm to 30 cm in water is needed to treat tumours located in depth in a patient. Since the Bragg peak position in depth is adjusted by the particle energy, the typical maximum energy is motivated by this. For protons, the typical maximum energy is about 250 MeV while for carbon ions the energy is about 400 MeV/u [141, p. 16]. This proton energy can be achieved in cyclotrons that have the advantage that they fit into a single large room, with separate treatment rooms, and are available from companies such as IBA [142] and Varian [143]⁽³⁾. However, carbon ions cannot be sufficiently accelerated in cyclotrons

⁽²⁾All numbers on the availability of particle therapy centres are extracted from the list provided by the Particle Therapy Co-Operative Group, which is available online [140].

⁽³⁾As measurements for this work are only performed with beams delivered by a synchrotron, the principle of a cyclotron is not explained here. For further information see for example [141].

available today and the more complex synchrotron is necessary. Particles are extracted from a source and then pre-accelerated in a LINAC followed by the injection into the synchrotron. The synchrotron itself is a circular accelerator, where particles are kept on a trajectory inside an evacuated beam pipe by deflecting and focussing magnets. Acceleration usually takes place only at one position with an RF cavity producing the accelerating electric field. The RF and the magnetic field need to be tuned when particles gain speed and energy during acceleration. When the desired energy is reached particles are extracted and sent via transfer lines to a treatment room. Usually there are three treatment rooms to optimise the use of the beam time of the accelerator, because the preparations such as patient positioning typically take more time than the actual treatment. Figure 5.2 shows the accelerator complex at CNAO.

5.1.4. CNAO

For this work, all measurements at a hadron therapy facility are performed at the Italian National Centre of Oncological Hadrontherapy (CNAO) ([144], [145]), which is located in Pavia, Italy. It is a synchrotron based facility (see section 5.1.3) with three treatment rooms. Currently, treatments with protons and carbon ions are possible but extension to ions such as Helium ions is planned. Table 5.1 gives an overview of the beam parameters⁽⁴⁾. A typical characteristic of a synchrotron beam delivery are the so-called spills: due to the needed working cycle of a synchrotron (filling, acceleration, extraction), the extraction is not continuous. At CNAO there is about 1 s beam (spill) followed by a break of 3 s. The beam delivery at CNAO is designed to be fully active, meaning that the volume of a tumour is ideally divided into slices in depth, which are irradiated by particles of the same energy. Active scanning of the beam – steered by deflecting magnets – is then applied to ‘paint’ a slice. A certain dose is given to a volume pixel (voxel) by directing a pencil beam⁽⁵⁾ to it, selecting the correct energy and deflecting the beam until the foreseen number of particles is reached and the next voxel is irradiated. However, it is impossible to irradiate only a single voxel: dose deposited to other voxels due to the Bragg curve shape and spread out of the beam needs to be taken into account.

Table 5.1.: Beam parameters at CNAO. Data are from [144], [146] and [147].

Beam particle species	p, C ⁶⁺
Beam range	3 g/cm ² to 27 g/cm ²
Bragg peak modulation steps	0.1 g/cm ²

⁽⁴⁾A list of beam sizes for different energies used for test measurements is given in table 5.4.

⁽⁵⁾The expression ‘pencil beam’ describes a relatively narrow beam.

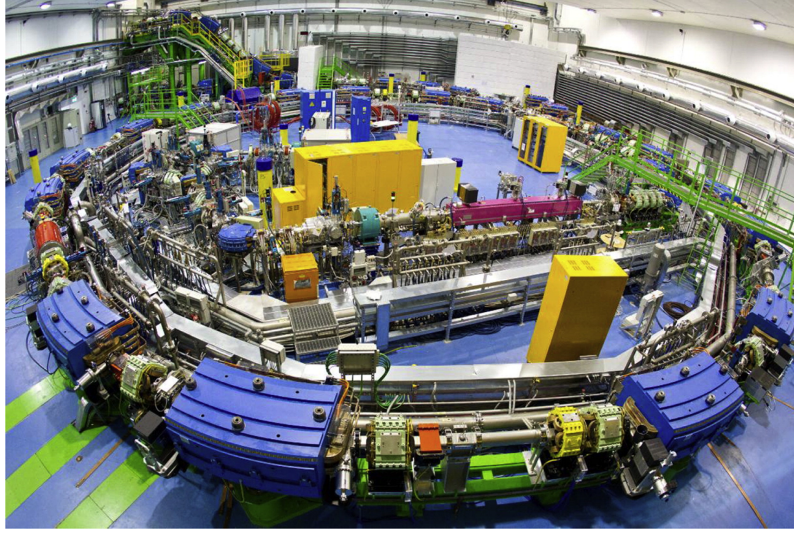
Table 5.1.: Beam parameters at CNAO (continued). Data are from [144], [146] and [147].

Range adjustment	0.1 g/cm ²
Adjustment/modulation accuracy	$\leq \pm 0.025$ g/cm ²
Energy range	60 MeV to 250 MeV (for protons) 120 MeV/u to 400 MeV/u (for carbon ions)
Energy step	0.02 MeV
Number of particles	10 ⁸ to 10 ¹⁰ per second during spill (for protons) 2 · 10 ⁶ to 2 · 10 ⁸ per second during spill (for carbon ions)
Average dose rate	2 Gy/min (for treatment volumes of 1000 cm ³)
Dose delivery precision	$\leq \pm 2.5\%$
Beam axis height (above floor)	120 cm
Beam size	4 mm to 10 mm FWHM for each direction independently
Beam size step	1 mm
Beam size accuracy	$\leq \pm 0.2$ mm
Beam position step	0.1 mm
Beam position accuracy	$\leq \pm 0.05$ mm
Field size	5 mm to 34 mm (diameter for ocular treatment) 2 × 2 cm ² to 20 × 20 cm ² (for H and V fixed beams)
Field position accuracy	$\leq \pm 0.5$ mm
Field dimension step	1 mm
Field size accuracy	$\leq \pm 0.5$ mm

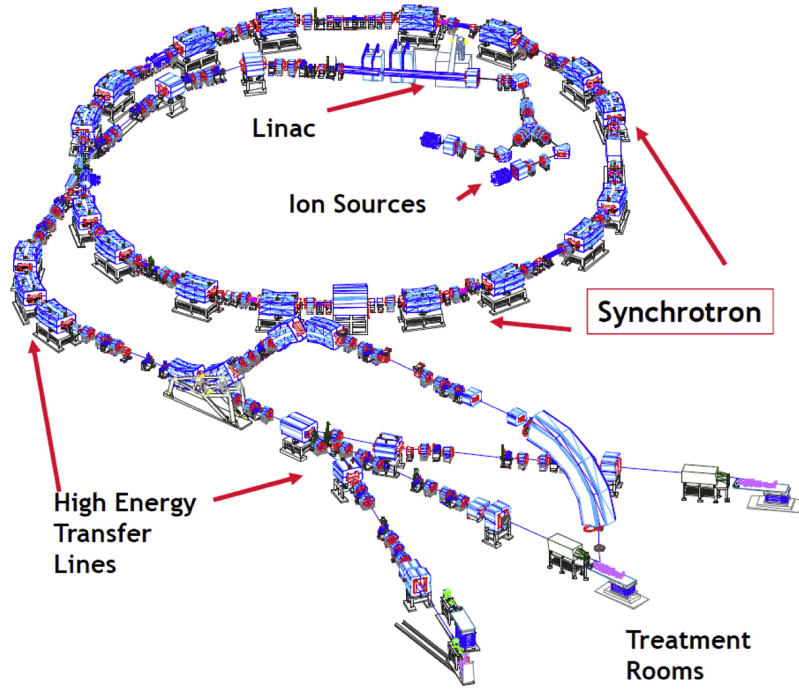
The beam delivery at CNAO is constantly monitored by the Dose Delivery System (DDS) [148]. In the nozzle⁽⁶⁾ there are two independent ionisation chambers as the main part of the DDS. These wide-area detectors measure the beam flux, position and width and are read out continuously at a certain frequency⁽⁷⁾. The control of the DDS provides not only the integrated delivered dose for each measurement but is also an important part of the interlock system that cuts the beam for example when there is a spot deviation larger than the set tolerance.

⁽⁶⁾The last part of the beam delivery system – before the beam goes into air – is often called nozzle. At CNAO it contains the DDS detectors, ripple filters and range shifters [148].

⁽⁷⁾For the measurements reported in this work the integration time is 50 ms with a negligible dead time between measurements.



(a)



(b)

Figure 5.2: Picture (a) of the CNAO accelerator complex and scheme (b) of the CNAO accelerator and beam delivery complex [144]. Ions are extracted from a source, then accelerated in a LINAC and a synchrotron and finally delivered via transfer lines to the treatment rooms.

The total dose per spot can be adjusted by the total number of particles and therefore by the irradiation time at a given instantaneous beam intensity. But also the instantaneous beam intensity is modified, and can be chosen from predefined intensity steps called for example F10 for 10% of the maximum intensity. F100, F50, F20 and F10 are available and have been checked for clinical commissioning to not affect other beam properties ([144], [16]).

Typically so-called ripple filters are used with carbon ions to produce a spread-out Bragg peak. A ripple filter consists of some material like Plexiglas with grooves such that the depth for the beam to pass through varies with position in the beam cross section and the Bragg curve in total is smeared out (see e.g. [149] for more information).

5.1.5. Treatment Planning

After the diagnosis of cancer and the choice of hadron therapy as the best treatment or one of the treatments, the treatment for the patient needs to be planned. The first step is to obtain information on the tumour and surrounding tissue by a computed tomography (CT) scan. With the help of these images, the target volume and other critical volumes such as organs at risk are defined. Also, the range of particles can now be predicted based on the anatomic structure and density. Then the desired dose in the tumour and the maximum acceptable dose for the surrounding tissue or organs are used to develop a treatment plan for the available machine. A treatment plan is the result of the optimised dose delivery and contains the treatment settings such as the entrance directions and dose delivered in each voxel. Figure 5.3 shows a comparison of treatment plans for protons and for photons.

5.1.6. Quality Assurance and Patient Treatment Plan Verification

A good treatment quality needs to be well assured as the beam is directed to patients. Any inadvertent irradiation of healthy tissue as well as under- or over-dosage of the treatment volume need to be avoided as this is highly dangerous for the patient. Therefore, there is a sophisticated system of regular checks of the beam delivery involving different measurements with various detectors and comparisons to reference values and simulations. Monitored quantities (and typical detectors used for these checks) are for example the Bragg curve (Physikalisch-Technische Werkstätten Dr. Pychlau GmbH (PTW) peakfinder, see section 5.1.7), the homogeneity of the scan field (EBT3 films) and beam monitor calibration (Farmer-type ionisation

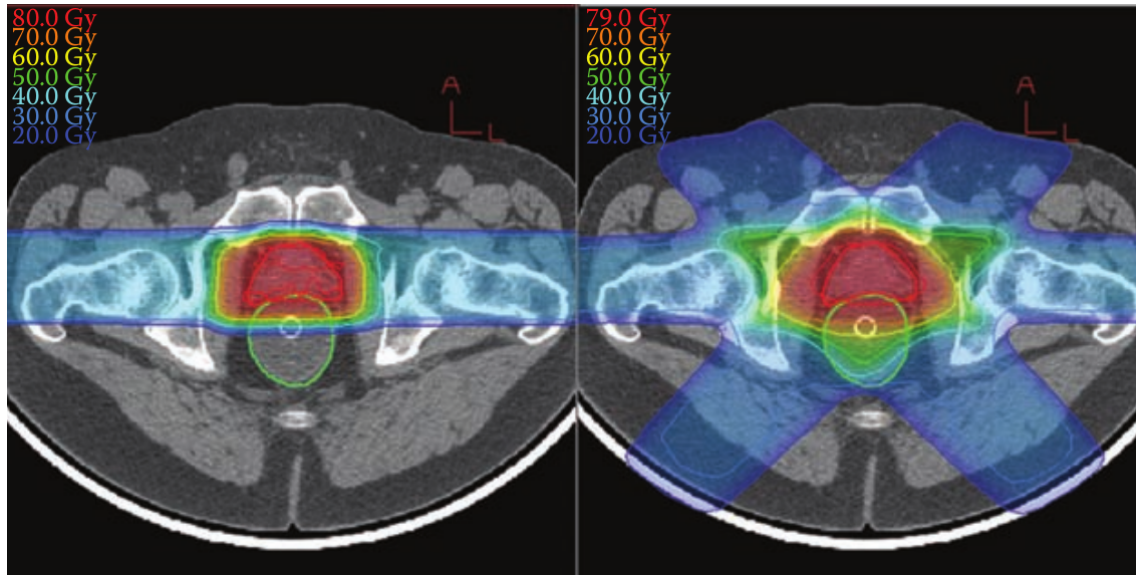


Figure 5.3: Comparison of a two-field treatment plan for protons (left) and a six-field plan for intensity modulated radiation therapy photons (right) for a prostate carcinoma [150, p. 184]. The planned dose contours are colour coded and the carcinoma is outlined in red.

chambers). These checks are performed at different frequencies, some of them even on a daily basis. The material that is irradiated for these checks often is water in a so-called water phantom, which is a plastic box filled with demineralised water and which is typically equipped with a motorised position system for a detector. This is for example used at CNAO on a daily basis to measure the energy deposition in a reference volume with a Farmer-type ionisation chamber. A detailed report on the quality assurance performed at CNAO can be found in [16].

Not only the machine parameters need to be well monitored but also a patient-specific quality assurance is necessary to ensure the high treatment quality. At CNAO the quality assurance procedure demands a verification of each treatment plan before the patient is treated ([151], [152]). For this, the water phantom is equipped with a block in which more than 20 small pin point ionisation chambers can be inserted. This block is then mounted on the motorised positioning system of the water phantom, the dose at known positions is measured and then compared to the predicted dose in the treatment plan. If measurements and plan match within a given tolerance, the plan is accepted. Figure 5.4 shows the tools used at CNAO for patient treatment plan verification.

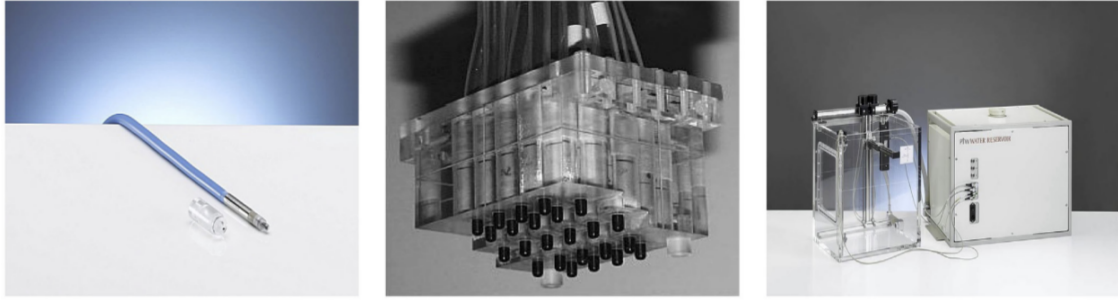


Figure 5.4: Tools for patient treatment plan verification at CNAO [152]: the PTW pin point ionisation chamber (left), the 3D block equipped with ionisation chambers (centre) and the PTW water phantom with an extra water tank (right).

5.1.7. The PTW Peakfinder

The peakfinder is the reference measurement tool used at CNAO to measure the Bragg curve and therefore is explained here. It consists mainly of two PTW ionisation chambers (very similar to the PTW 34080 ionisation chamber acquired for the integrated system developed in this thesis and described in section 5.4), a closed water column and needed supplies and readout. One ionisation chamber is the reference chamber in front of the water column and the other one is the measurement chamber. The amount of water between the two chambers (i.e. the depth in water of the measurement chamber) can be changed to perform a depth scan and to measure the Bragg curve. Positions in water from 20 mm to 350 mm are possible with a spatial resolution of 10 μ m. Typical dose uncertainties are less than 1%. Figure 5.5 shows a scheme of the peakfinder.

5.2. Motivation

Although hadron therapy is clinically established, improved detectors for dose measurements and quality assurance are needed [154, p. 216]. At CNAO, the main interest is in the improvement of the patient treatment plan verification since the machine quality assurance is well established and sufficiently convenient [147]. The active scanning performed with magnets is a challenge for dosimetry as the scanning speed is too fast to have the detector following it on a positioning system. Therefore the whole area that is ‘painted’ by the beam needs to be instrumented with a sufficient spatial resolution. Arrays of detectors or the 3D block of ionisation chambers for patient treatment plan verification at CNAO (see section 5.1.6) are

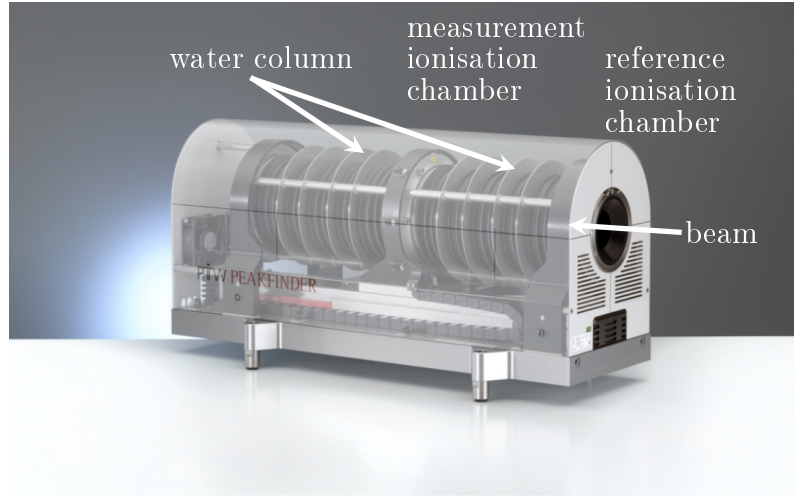


Figure 5.5: The PTW peakfinder [153] is a commercial quality assurance tool to measure Bragg curves. Annotations added by the author.

a typical approach to overcome this problem. However, the spatial resolution and the number of measurement points is limited due to the smallest possible size of the ionisation chambers, which is around 5 mm. A detector that could provide reliable measurements with a higher spatial resolution covering ideally the maximum irradiation field and the typical volume irradiated during a treatment would be a huge improvement. GEMs can be a basis for such a detector as they can be built sufficiently large ($20 \times 20 \text{ cm}^2$) and provide a good spatial and temporal resolution while not being too expensive. The Timepix provides a superior spatial and temporary resolution with the ASIC alone not being too expensive. However, currently the readout area is limited to the quad version used in this work, which is about $3 \times 3 \text{ cm}^2$.

The first steps to demonstrate the capabilities of the GEMPix are to investigate the accuracy of the detector by measuring the Bragg curve, comparing it to simulations and to provide a 3D reconstruction of the energy deposition. This is presented in the following sections.

5.3. Measurements with the CNAO Water Phantom

In a first set-up the GEMPix is mounted on the water phantom used at CNAO for quality assurance and the DDS is used as a reference detector. Better data quality is achieved with the integrated system (see following sections). However, results

obtained with the set-up using the CNAO water phantom are briefly presented in this section as they are the main motivation to develop the integrated system and to simulate the full set-up in FLUKA.

5.3.1. Set-up

Figures 5.6 and 5.7 show the set-up. Measurements are performed at CNAO in treatment room number 3 with a fixed horizontal beam line. The GEMPix is facing directly the beam. It is installed in a water tight Poly(methyl methacrylate) (PMMA) box mounted on the motorised positioning system of the water phantom used for quality assurance at CNAO (MP3-P, PTW [16], see also figure 5.4). The depth axis (parallel to the beam) has a range of movement of more than 350 mm and a position reproducibility of ± 0.1 mm. Measurements are performed with pencil beams of carbon ions (C^{6+}) with a kinetic energy of 280 MeV/u or 332 MeV/u. Only for the linearity study (see section 5.3.2), a flat field is used instead of a single pencil beam. The lowest instantaneous beam intensity commissioned for clinical applications, F10, is used (see section 5.1.4), which is about $2 \cdot 10^6$ particles per second during spill. The spill duration is about 1 s, followed by a break of 3 s. The beam profile in air just before entering the phantom is in both dimensions approximately Gaussian with $\sigma = 2$ mm.

5.3.2. Measurements and Results

Linearity Check

A linearity check of the GEMPix response is performed with a 60×60 mm² scanned flat field that is chosen larger than the GEMPix to avoid any possible edge effects. Carbon ions with a kinetic energy of 280 MeV/u are used and the total number of particles is varied. Figure 5.8 shows the linearity of the response over a factor of five in the total number of delivered particles, matching approximately the expected peak-to-plateau ratio in a Bragg curve. The applied uncertainty is estimated to be 1%, which is approximately the uncertainty obtained during the depth scan measurements. Note that here the total number of particles and not the instantaneous beam intensity is changed.

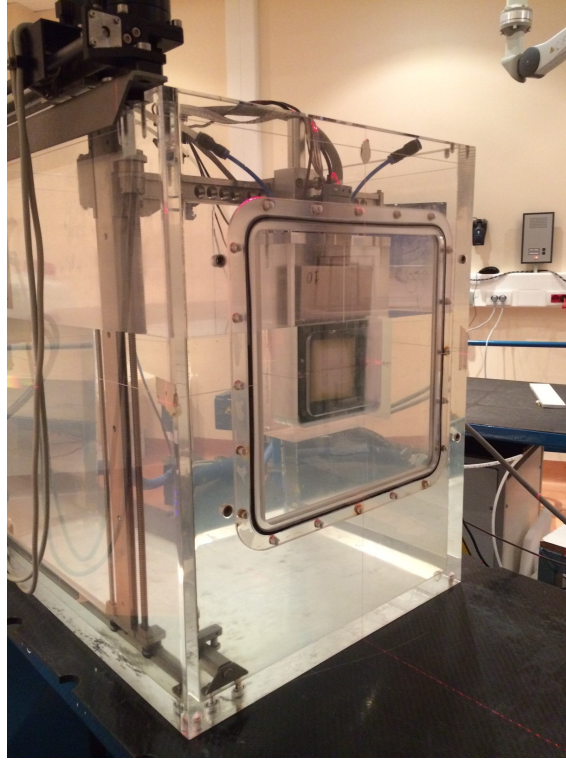


Figure 5.6: The GEMPix mounted on the water phantom used at CNAO for quality assurance [126].

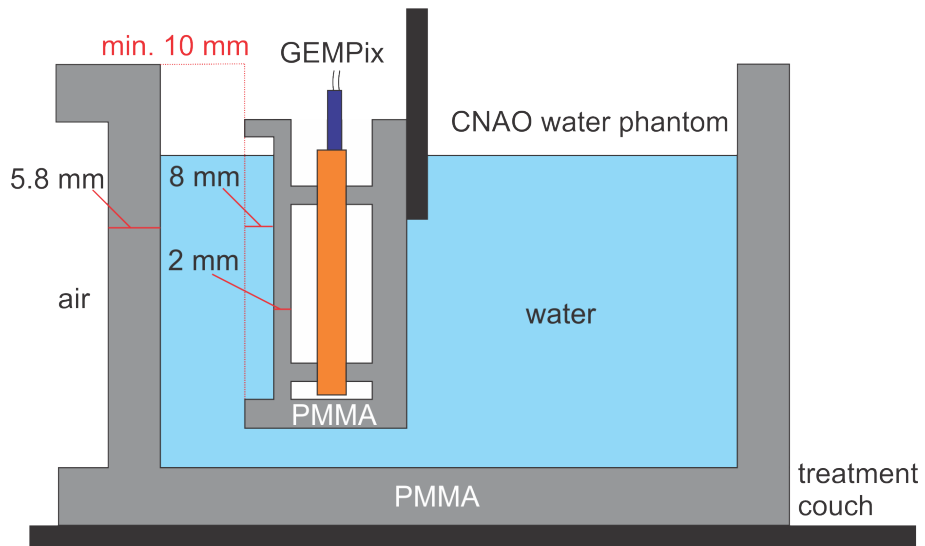


Figure 5.7: Scheme (not to scale) of the GEMPix mounted on the water phantom used at CNAO for quality assurance [126].

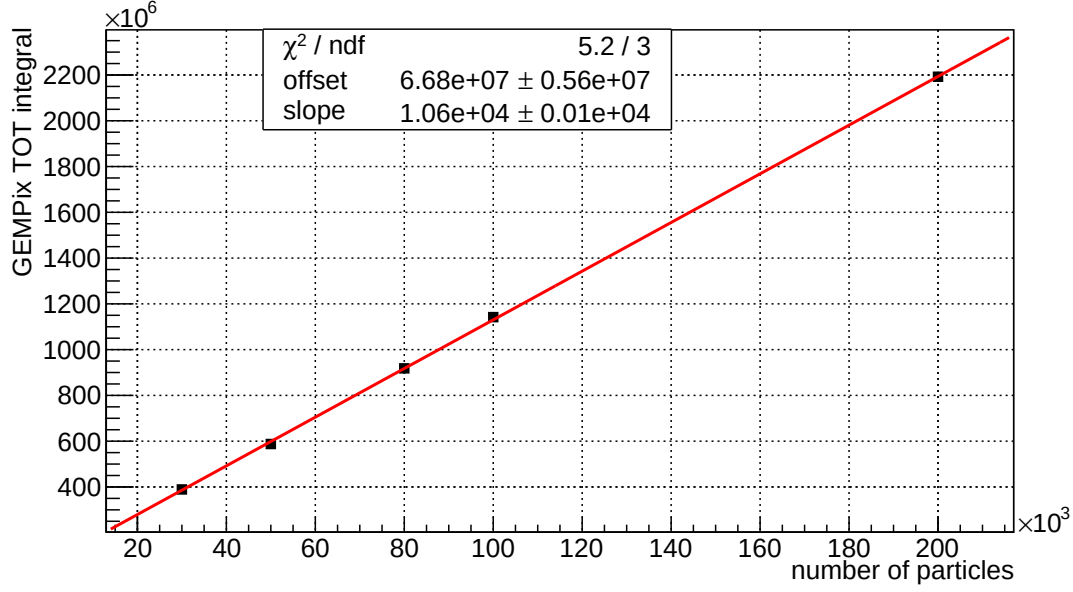


Figure 5.8: The GEMPix response is linear from $3 \cdot 10^4$ to $2 \cdot 10^5$ delivered particles. Uncertainties are smaller than the data points [126].

Depth Scans

The depth is varied from the minimum possible depth (about 26 mm water equivalent thickness) to a position well beyond the Bragg peak. Usually about 30 positions in depth are used, while the distance between positions is chosen smaller in regions of rapid change in the Bragg curve, i.e. close to the Bragg peak and on the distal edge. The measurements at each position last 30 s, which results in about 15 min for the total depth scan. The frame length is 50 ms, the same as the integration time of a DDS measurement. Due to data readout and pixel reset, a dead time of 100 ms to 300 ms between frame acquisitions occurs⁽⁸⁾. Each frame of the GEMPix is a 2D measurement of the energy deposition. Figure 5.9 shows such single frames. The elliptical shape of the beam at small depths in water is expected due to the slow resonant extraction of the beam from the CNAO synchrotron ([155], [147]), while at larger depths the influence of the scattering of the particles traversing through the water is dominant and leads to a more circular shape.

The Bragg curve is calculated from the measured GEMPix frames and the DDS reference values. DDS values are needed to normalise the GEMPix results to the delivered beam intensity: the beam intensity does not only alternate between ‘spill’

⁽⁸⁾The reset is done for every second frame and takes about 200 ms so that the dead time between frames alternates between 100 ms and 300 ms.

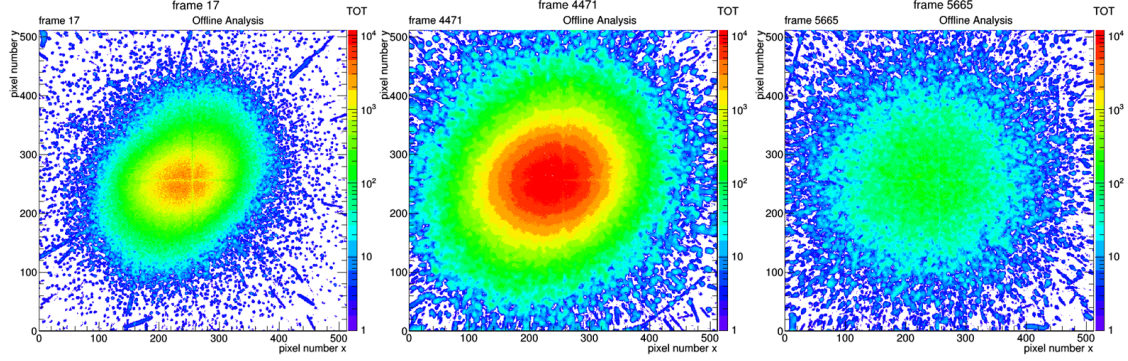


Figure 5.9: The superposition of single particle tracks in the GEMPix – integrated during one frame length – produces typical images as measured in the beam entrance (left), the Bragg peak (centre) and the tail (right) [126]. The x and y axes represent the spatial coordinates given in units of pixel number. The 512×512 pixels cover an area of $2.8 \times 2.8 \text{ cm}^2$ as each pixel is $55 \times 55 \mu\text{m}^2$ large. The measured TOT value in each pixel, approximately proportional to the deposited energy, is colour coded.

and ‘no spill’ but also varies substantially during a specific spill. Therefore an ideal reference value would be measured synchronously with the GEMPix measurement. However, a trigger system between GEMPix and DDS does not exist but both measurements run independently with a mismatch between computer clocks of the two systems, making an alignment and smoothing necessary. First, the TOT counts in a single GEMPix frame are summed up yielding a single number per frame. Then, the time between GEMPix and DDS is coarsely aligned in 50 ms steps and the time shift leading to the smallest difference between the two systems is chosen. Figure 5.10 shows that GEMPix and DDS measurements match well after coarse alignment and both follow the typical spill structure of the synchrotron. The average of the two DDS measurements closest in time to a GEMPix measurement is calculated and the ratio between GEMPix measurement and DDS average is taken to obtain the normalised TOT counts for a single frame. Since about 15 frames per position are acquired, the average of the ratios at the same position is calculated. The sigma on the mean value of the average of the ratios is used as the uncertainty for the result and is typically 1 to 2%. The average ratio is then – except for a common normalisation factor of the whole Bragg curve – one point of the Bragg curve. Figure 5.11 shows a Bragg curve compared to a reference measurement with the PTW peakfinder. A general normalisation factor for the GEMPix measurements is applied to match the reference measurement in the Bragg peak. This normalisation is chosen somewhat arbitrarily and any other point chosen to match the two curves is valid as well. The difference between GEMPix and reference measurement is up to 15% in the entrance

plateau and the peak while the differences in the tail are larger. Differences stated are only relative and depend on the choice of normalisation.

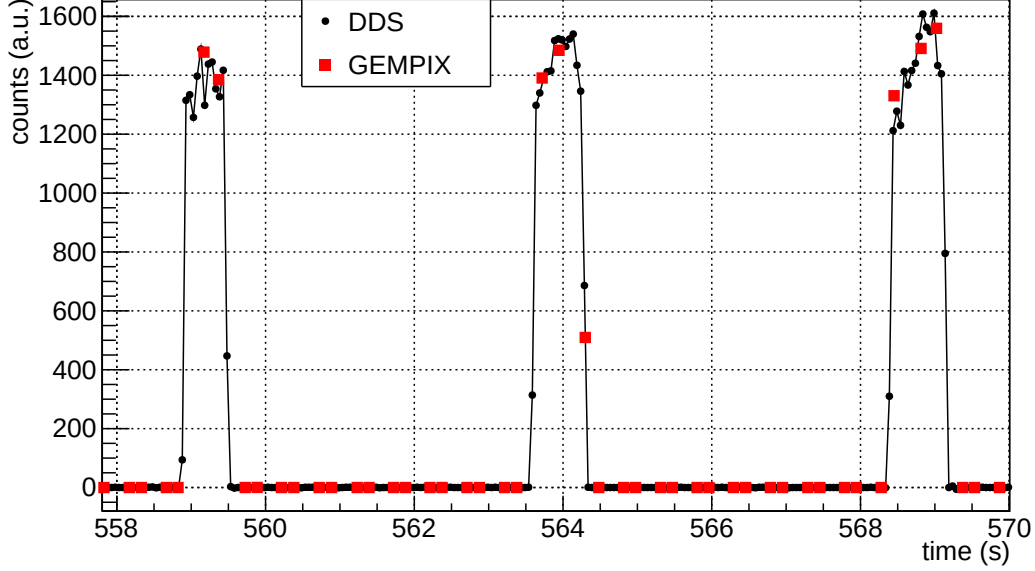


Figure 5.10: After time alignment, DDS and GEMPix measurements match well and the typical spill structure is visible [126]. A general normalisation factor only for this visualisation is applied to the GEMPix counts to approximately match the DDS counts. The time is given from the start of the measurement.

5.3.3. Discussion

The measured Bragg curve in figure 5.11 is smooth and shows all expected features of a Bragg curve: a medium dose in the entrance plateau, followed by the Bragg peak and a sharp distal fall-off towards a small dose in the tail. The overall shape matches the peakfinder measurement. However, there are differences compared to the reference measurement with the PTW peakfinder that are too large for clinical applications. The main reasons that have been investigated are:

- The settings of the GEMPix are not ideal. As presented in section 5.7.3 for the integrated system, the signal in the GEMs matches the expectation. However, the produced charge is split on a large number of pixels and for each pixel a threshold is applied. The effect of this threshold cut changes with depth as the energy deposition per primary particle changes and therefore is not

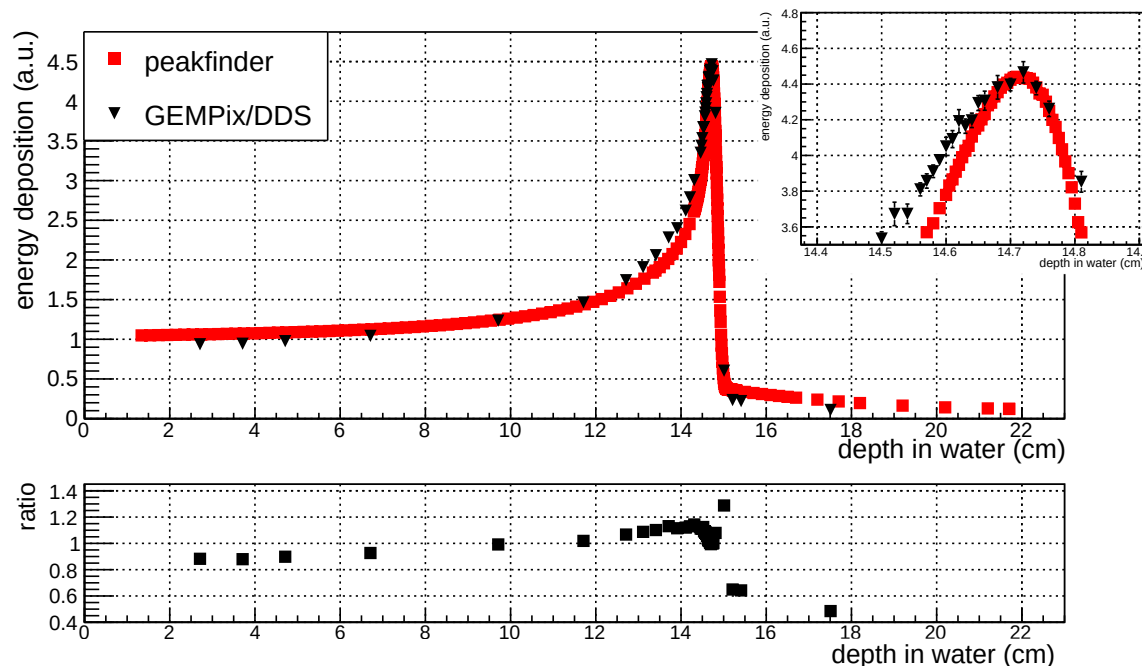


Figure 5.11: The Bragg curve (top, inset showing a zoom to the Bragg peak region) measured with the GEMPix and normalised to the reference DDS measurement (black) and measured with the PTW peakfinder (red) [126]. The bottom plot shows the ratio of the two measurements. The Bragg peak is observed at a depth some 3 mm in front of the expected position of 150 mm as two ripple filters are used.

compensated by the general normalisation factor. A lower effective threshold is applied later with a more careful detector set-up.

- The accuracy of the naive comparison between GEMPix and PTW peakfinder is – especially in the tail – limited by the different sensitive area perpendicular to the beam axis of the two devices: the PTW peakfinder’s measurement ionisation chamber has a diameter of about 8 cm. The GEMPix has an area of only $2.8 \times 2.8 \text{ cm}^2$. With increasing depth in water, the beam spreads out and the losses for measurements with the GEMPix become significant, especially in the tail (see FLUKA simulation in section 5.6.5).
- No temperature correction for the GEMPix is applied. Since the depth scans are always performed from smaller to larger depth, the heat-up of the readout could have a systematic effect: a test measurement with an ^{55}Fe source in the laboratory showed an increase in the GEMPix response of up to 5% within the first 10 min after starting a measurement. Later, the correction introduced

in section 3.4.5 is applied and the readout is started before the actual start of the measurement (see section 5.4.2).

- The different stopping power of the filling gases – air in the ionisation chambers of the PTW peakfinder and Ar:CO₂:CF₄ (45:15:40) in the GEMPix – affects the energy deposition: a 4% underestimation in the Bragg peak has been measured with 270 MeV/u carbon ions when comparing an Argon filled detector to an air filled one [156]. A similar effect is obtained when calculating the difference of air to Ar:CO₂:CF₄ (45:15:40) with SRIM [10].
- As explained above the time between GEMPix and DDS measurements needs to be adjusted. Although the effect of the time adjustment on the results is limited by the smoothing applied to the DDS, it still leads to increased fluctuations of the results. A systematic effect depending on the depth is not expected but could also not be completely ruled out, calling for an improved normalisation procedure.

5.3.4. Conclusions of the Measurements with the CNAO Water Phantom

The results presented in this section motivate a couple of improvements: so most importantly the integrated system is developed to provide a dedicated triggerable normalisation measurement and to gain full control of all measurement components, for example to be independent from the CNAO water phantom and DDS. The complete experimental set-up is implemented in a FLUKA simulation to study the crucial effect of the relatively small GEMPix area. Furthermore, the settings of the GEMPix are studied in more detail and properly adjusted.

5.4. The Integrated System

The ‘integrated system’ is developed after preliminary measurements at CNAO called for improvements, as described in section 5.3. A system is achieved that provides better data quality – for example regarding the reference measurements –, does not need a trigger from the treatment centre, provides an online analysis and can be set up easily and fast.

5.4.1. Hardware

The integrated system consists of a commercial water phantom, a commercial ionisation chamber as a reference detector, the GEMPix, a trigger system and other necessary equipment like laptops, cables and power supplies. Figure 5.12 shows a scheme of the integrated system. The system is designed to be set up relatively fast by collecting for example all supplies and readouts on a trolley.

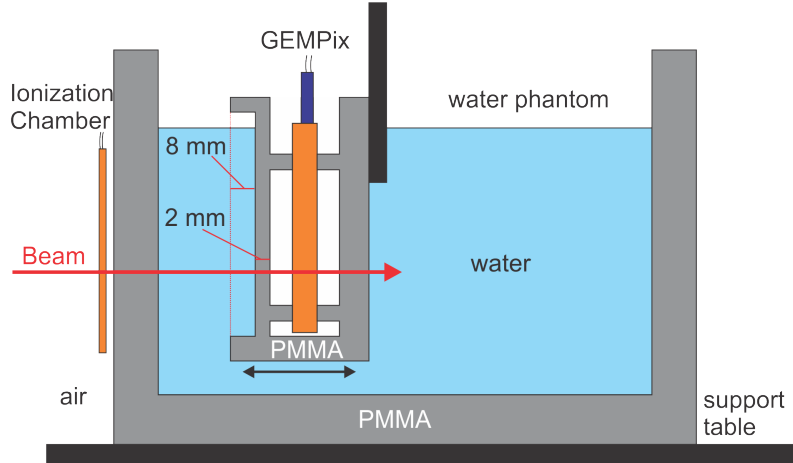


Figure 5.12: Scheme of the integrated system (not to scale). The beam passes through the ionisation chamber before entering the water and the GEMPix.

Water Phantom The Luzerner Kantonsspital (Lucerne Canton Hospital, [157]) in Lucerne, Switzerland, donated a water phantom used before for quality assurance measurements in the X-ray radiation therapy group at the hospital. The water phantom is an IBA Scanditronix Wellhöfer Blue Phantom type 2001. The inner dimensions of the water tank are approximately $62 \times 65 \times 53 \text{ cm}^3$. The maximum moving range is 48 cm in each dimension with a smallest step size of 0.1 mm. An absolute (re-)calibration and correction of the positioning system via approaching and measuring the mechanical endpoints exists. The needed power supply and control (CU 500 E) for the positioning system was also donated, as well as an external water tank with pump and control WP600. More than 150 l of demineralised water are stored in this tank and pumped into the water phantom when needed. The filling takes about 10 min. The support table (manual lift table type 3023) for the phantom can be adjusted in height manually such that no other support is needed to match the height of the beamline. Phantom support table and water tank are on rolls to enable fast set-up. Figure 5.13 shows the water phantom and the trolley for electronics at CERN's calibration laboratory.

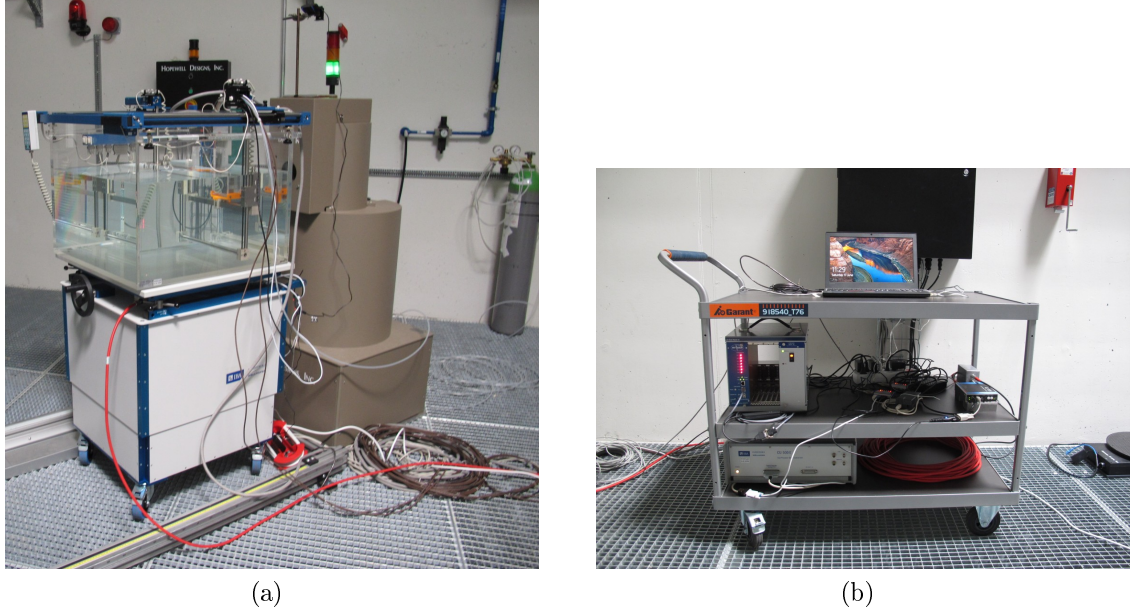


Figure 5.13: (a) The water phantom is placed in front of a source holder for radioactive sources at CERN's calibration laboratory. The gas bottle to supply Ar:CO₂:CF₄ (45:15:40) can be seen in the background. (b) The trolley for the needed electronics can be placed up to 10 m away from the water phantom to be moved out of the direct radiation field. Only one usual power outlet and an internet connection to enable remote control of the PC are needed.

Ionisation Chamber The ionisation chamber for the normalisation to the beam intensity is acquired from PTW, Germany. It is a thin window ionisation chamber of type PTW 34080 with an electrode diameter of 81.6 mm and a window thickness of only 0.62 mm and 1.16 mm, totalling to an area density of 72 mg/cm². It is vented to air with a nominal sensitive volume of 10.5 cm³. An HV of 400 V is applied, yielding a nominal response of 325 nC/Gy when irradiated with ⁶⁰Co. The PTW peakfinder uses two very similar ionisation chambers (only with a thicker window for the use in water). A temperature and pressure correction given by PTW is applied⁽⁹⁾:

$$k_{TP} = \frac{(273.2 + T) \cdot P_0}{(273.2 + T_0) \cdot P} \quad (5.1)$$

where T is the temperature in degree centigrade, T_0 the reference temperature (here: 20 °C), P the pressure (in hPa) and P_0 the reference pressure (here: 1013.25 hPa). To obtain the corrected value, the measured value is multiplied by k_{TP} . Figure 5.14a

⁽⁹⁾This is a common correction for ionisation chambers (see for example [19, p. 326]).

shows a picture of the ionisation chamber and more specifications can be found in table A.4.

Ionisation Chamber Readout The ionisation chamber is powered and read out by the Pyramid Technical Consultants (PTC) IC101. It supplies the ionisation chamber with the needed 400 V (adjustable), has a dynamic range of <1 pA to 200 μ A and is connected to a laptop via USB (RS-232 plus an adaptor to USB). A TTL signal can be used as external trigger. Figure 5.14b shows a picture of the IC101 and more specifications can be found in table A.5.

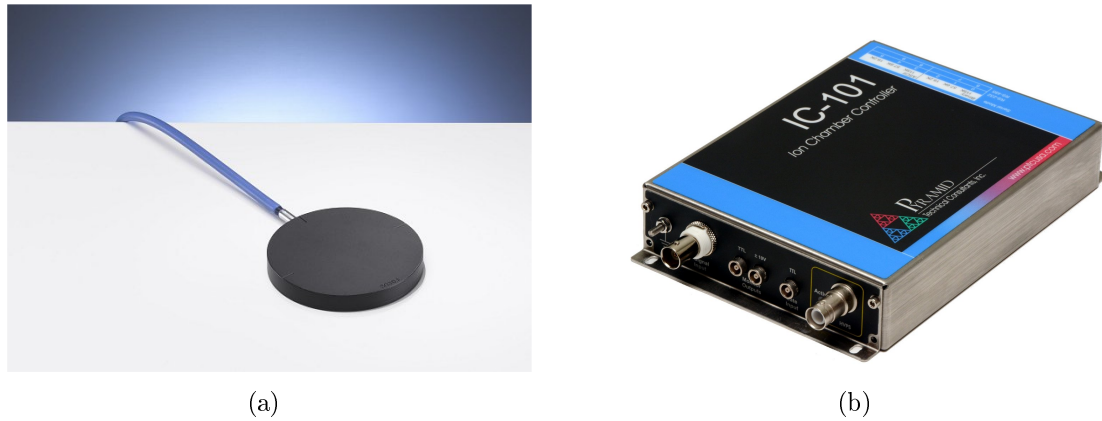


Figure 5.14: Pictures of (a) the PTW 34080 ionisation chamber [158] and (b) the PTC IC101 ionisation chamber readout [159].

Cabling Readout and supplies for the detectors are kept on a trolley in a distance from the water phantom to avoid any radiation damage. All cables between the water phantom and the trolley are at least 10 m long to have enough flexibility to place the trolley anywhere in the treatment room. Most of the cables can be produced or acquired at this length relatively easily (power cable; USB cable with active signal repeater and USB hub at the phantom; LV, HV and trigger signal cable for the GEMPix; water phantom control and supply cable; gas tube). However, the signal cable (BNC) for the ionisation chamber cannot simply be extended over such a long range. A custom solution with adaptors on both ends using a SPA6 cable is built in the CERN radiation protection group⁽¹⁰⁾.

Trigger System A simple solution is implemented based on an Arduino [161]. It can support two TTL output signals used to start the measurement of the ionisation

⁽¹⁰⁾The SPA6 cable [160, p. 39] was developed at CERN for operation of ionisation chambers over long distances in the LHC tunnel.

chamber and the GEMPix. The timing accuracy of the output signals is sufficient to synchronise measurements of $\mathcal{O}(10\text{ ms})$ with less than 1% uncertainty.

GEMPix and Ionisation Chamber Holder The same water tight box for the GEMPix is used as before for measurements with the CNAO water phantom. However, a new connection between the water phantom's positioning system and the box is necessary. The ionisation chamber needs to be mounted on the water phantom as well. One holder for the GEMPix and one for the ionisation chamber are designed and produced with a 3D printer at CERN's Ideasquare [162]. Figure 5.15 shows pictures of the printed holders.

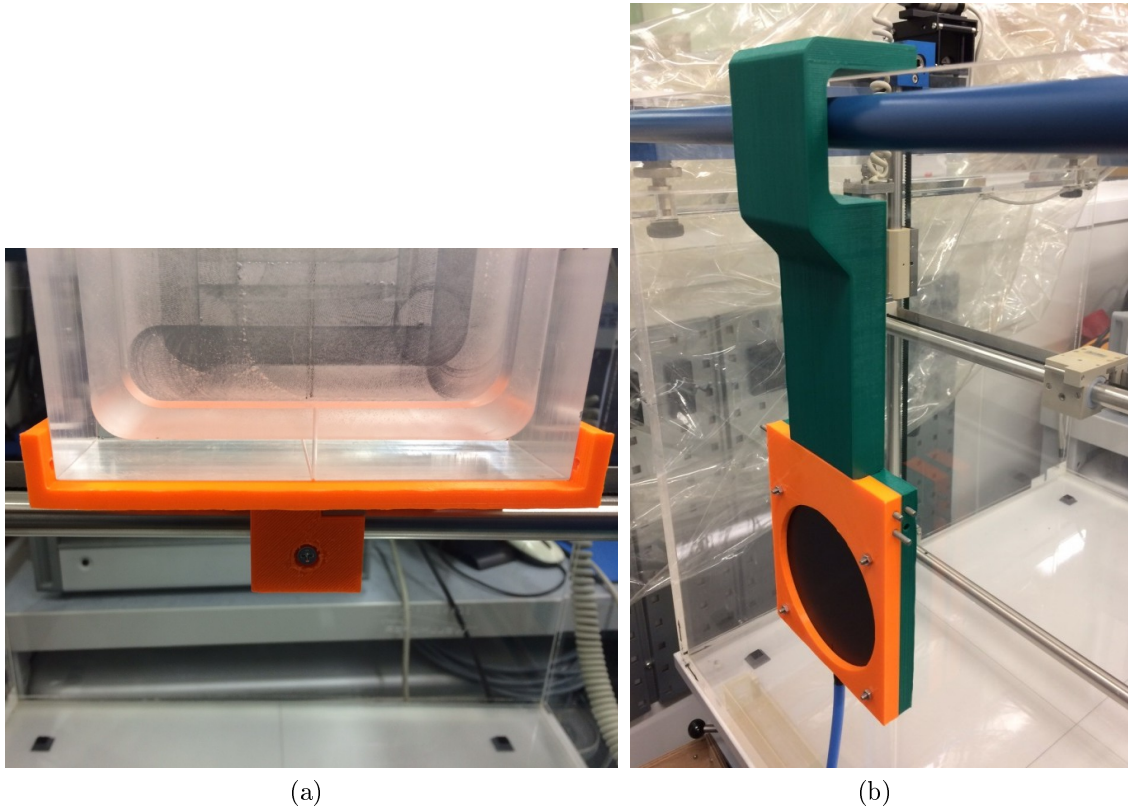


Figure 5.15: Pictures of (a) the holder for the GEMPix (the orange part) and (b) the holder of the ionisation chamber (orange and green parts) printed at CERN's Ideasquare.

Slow Control A yoctopuce meteo sensor (the same as used inside the GEMPix) is placed on the phantom to monitor ambient temperature and pressure for correction of the ionisation chamber current.

5.4.2. Control Systems and Data Acquisition

A laptop with Windows operating system [163] is placed on the trolley for the control and data acquisition. It is connected via Ethernet to the control room where another laptop with Linux operating system (Ubuntu [164]) enables remote control of all systems and the data acquisition. The choice of the operating systems is driven by the availability of system drivers, basic control functions and Pixelman for Windows and data analysis programs such as ROOT and Python preferably for Linux. A considerable amount of work is required to implement all controls. Basic controls of the suppliers such as for the ionisation chamber readout or functionalities in commercial software for the water phantom are used as a start. Due to the best availability of software snippets from the companies, LabVIEW is chosen for all control systems.

The **ionisation chamber control** is able to perform a calibration with the internal current source, perform measurements with various different settings and plot the results online. Either an internal trigger can be used to measure independently or an external trigger can start and stop the measurement. Data are written to a simple text file containing the time stamp, the current measurement and the trigger count. The value of the HV can also be adjusted. Figure 5.16 shows a screenshot of the control.

To implement and modify the code for the **trigger control** on the Arduino, the Arduino software (IDE) is used. Once loaded on the Arduino, the communication – the order to start or stop sending triggers – is performed by LabVIEW.

The **control of the positioning system** is used in three different steps: first, the limits for the movement are defined⁽¹¹⁾. Especially the height limit needs to be checked carefully depending on the water level. For assembly, testing or fine tuning to the beam axis, the positioning system can be moved to any desired position in the limits by either a simple software control or by a button control attached to the phantom. For depth scans, the positioning is performed automatically according to the pre-defined positions. Figure 5.17 shows a screenshot of the control.

An **HV control** for the GEMPix existed already but is modified to produce a log file (text file) containing all HV values and the temperature, pressure and humidity inside the GEMPix gas. If desired, the online HV correction is possible. See also section 3.4.5.

⁽¹¹⁾There are different levels of limits: on the highest level, it is ensured that the positioning system cannot collide with the walls of the phantom. Only a lower level is changed here to prevent the larger GEMPix box from colliding with the walls. Most importantly, the height is limited so that no water can flow into the GEMPix box as the box is open on top.

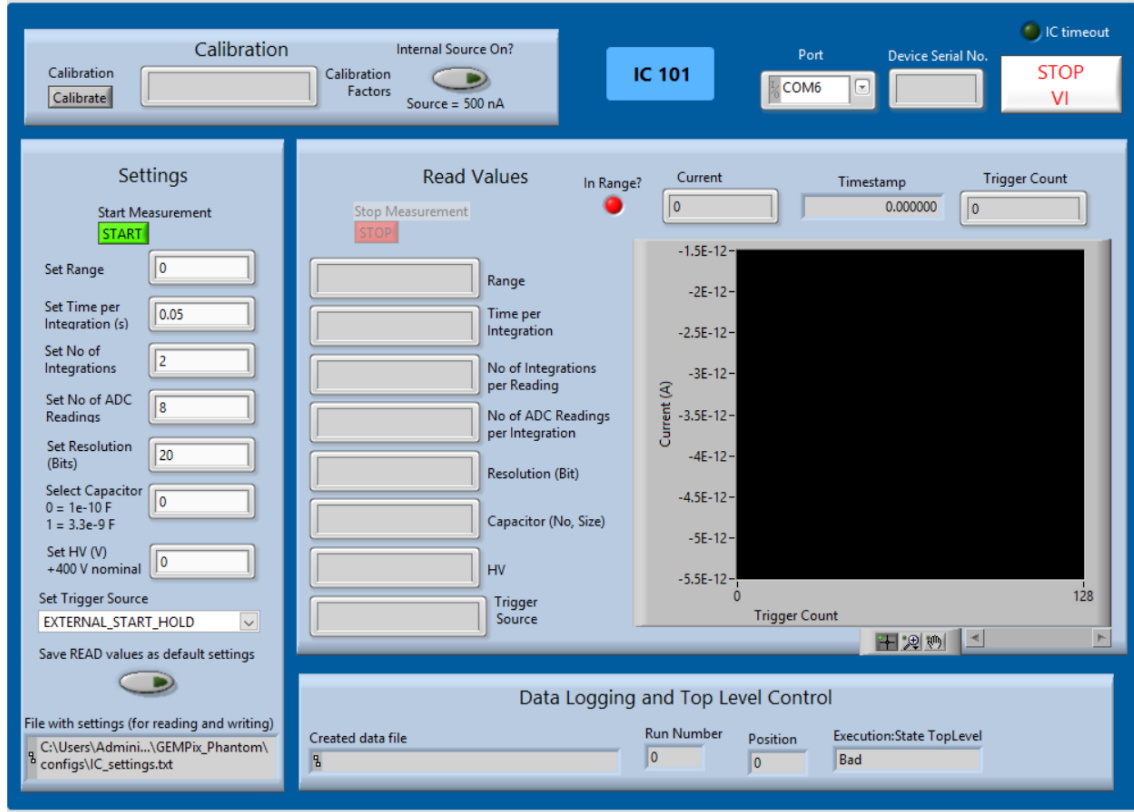


Figure 5.16: Screenshot of the ionisation chamber control written in LabVIEW. Calibration (top), adjustment of settings (left), online result display (right) and data storage (bottom) are supported.

The ambient temperature, pressure and humidity values are written every 10 min in a log file (text file containing these three values and a time stamp) by the **slow control**.

Finally, the **top level control** can control all necessary subsystems (e.g. the LabVIEW programs explained above) except for limited interaction with the Pixelman control for the GEMPix. Figure 5.18 shows a screenshot of the control. It is designed to perform automatic depth scans. Therefore, the first step is to check if the GEMPix HV control is running. As this does not need to be changed for each depth scan, no further interaction is implemented. Then, the actual settings for the depth scan such as the number of positions and a set of pre-defined positions are chosen (block '1' in figure 5.18). The settings of the GEMPix need to be changed for each new run in Pixelman but are then stored in a text file and read in by the top level control. Pixelman can be started from the top level control (block '2' in figure 5.18). This process already starts the GEMPix readout to reach the temperature equilibrium,

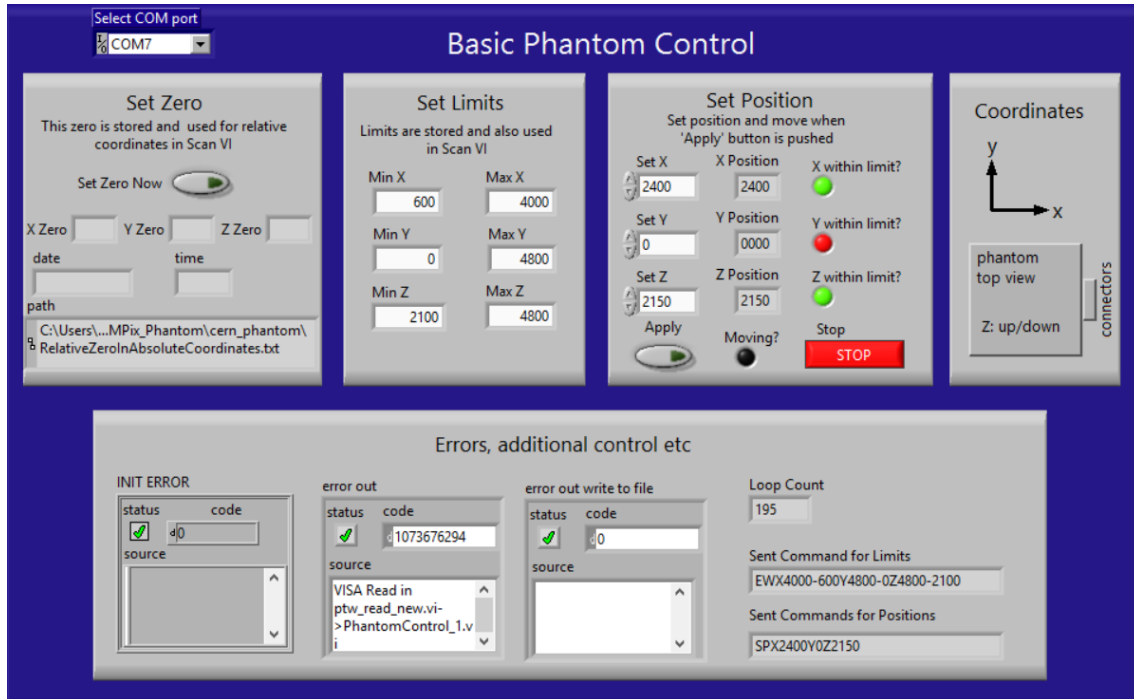


Figure 5.17: Screenshot of the water phantom control: A reference (‘zero’) value is chosen for relative coordinates during a depth scan (‘Set Zero’ block) after the limits of the control have been set with another control (limits are displayed in the ‘Set Limits’ block). The positioning system can be moved to any position in the limits (‘Set Position’ block). An explanation of the used coordinates (right) and an error display (bottom) are also provided.

but data are discarded until the run is started. The user is asked for completion of this step (block ‘3’ in figure 5.18). The phantom positioning system will move to the first position and controls in the top level control will light green when the system is ready. The user is asked to start the online analysis (block ‘4’ in figure 5.18, see also section 5.4.3).

When the run is started, the system will start the following procedure:

1. Phantom positioning control: move to desired position, send ‘phantom ready’ and ‘position’.
2. Ionisation chamber control: receive ‘phantom ready’ and ‘position’, create new file for this position, send ‘IC ready’ and wait for triggers.
3. Pixelman: receive ‘IC ready’, wait for triggers and send ‘Pixelman ready’.

4. Trigger control: receive ‘Pixelman ready’ and read number of ‘triggers per position’, send triggers until ‘triggers per position’ is reached and then send ‘move to next position’.
5. Phantom positioning control: receive ‘move to next position’.

Then the procedure is repeated until the last position is reached, while the status and, for example, the measured ionisation chamber current are displayed.

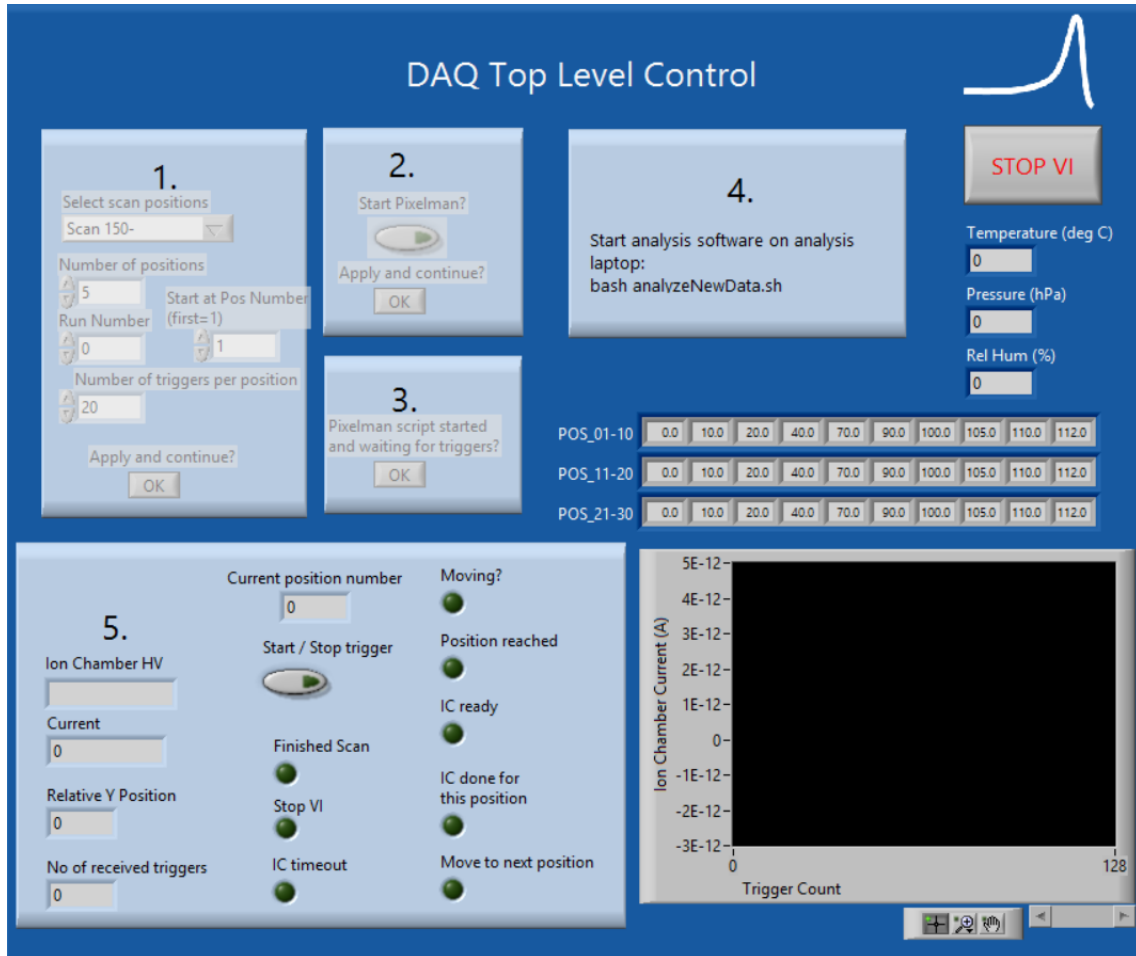


Figure 5.18: Screenshot of the top level control. See text for further explanations.

All controls are designed to work under the top level control but also in stand-alone. In this way, other measurements than the usual depth scans are possible with manual control of the subsystems. An extension to the automatic system that can be implemented relatively easily, would be to trigger only during spill. Since the signal of the ionisation chamber during spill and during no spill differs by a factor of 10 to 100, a simple threshold could be applied to decide whether to send out triggers.

5.4.3. Online Data Analysis

Data are stored locally on the laptop in the treatment room. The online data analysis should be started on the laptop in the control room when the actual measurements are started. As soon as the data acquisition at a certain position is finished, the online analysis copies the data to the analysis laptop in the control room and starts the analysis. A shell script manages all subroutines, which are written in Python or C++. It also takes care of the folder structure and – in case an analysis is redone – deletes old files after asking for permission. Only the number of the run to be analysed needs to be stated when the programme is started; the position number, the depth and other information are then automatically retrieved. In a first step, data from the GEMPix need to be converted from the initial binary format into ROOT files⁽¹²⁾. GEMPix data are analysed using a script written in the Mafalda framework (see section 2.4.2). For the online analysis most of the capabilities such as the frame viewer are disabled and the main task is to calculate the sum of the TOT counts of all pixels. At this step, all relevant information is stored in small text files containing the measurement number and the measured value for the GEMPix and the ionisation chamber. The ratio of each GEMPix measurement to the corresponding ionisation chamber measurement is calculated and the average of all ratios for a certain position gives the final number which is a single point on the Bragg curve. The assigned uncertainty on the average is calculated from the sample variance. For the online analysis, no further normalisation or depth correction is applied, but the direct plot of energy deposition against depth is displayed. Figure 5.19 shows a screenshot of the online analysis.

5.5. Test Measurements with the Integrated System

The integrated system is carefully tested before the first measurements with the complete system at CNAO. A test studying the delay of the GEMPix when triggered externally is described in section 3.4.6. The tests described here focus mainly on the ionisation chamber. As this is used for the normalisation, any malfunctioning would have a direct impact on the depth scan results and had to be ruled out.

⁽¹²⁾This converter was written by John Idarraga from CERN.

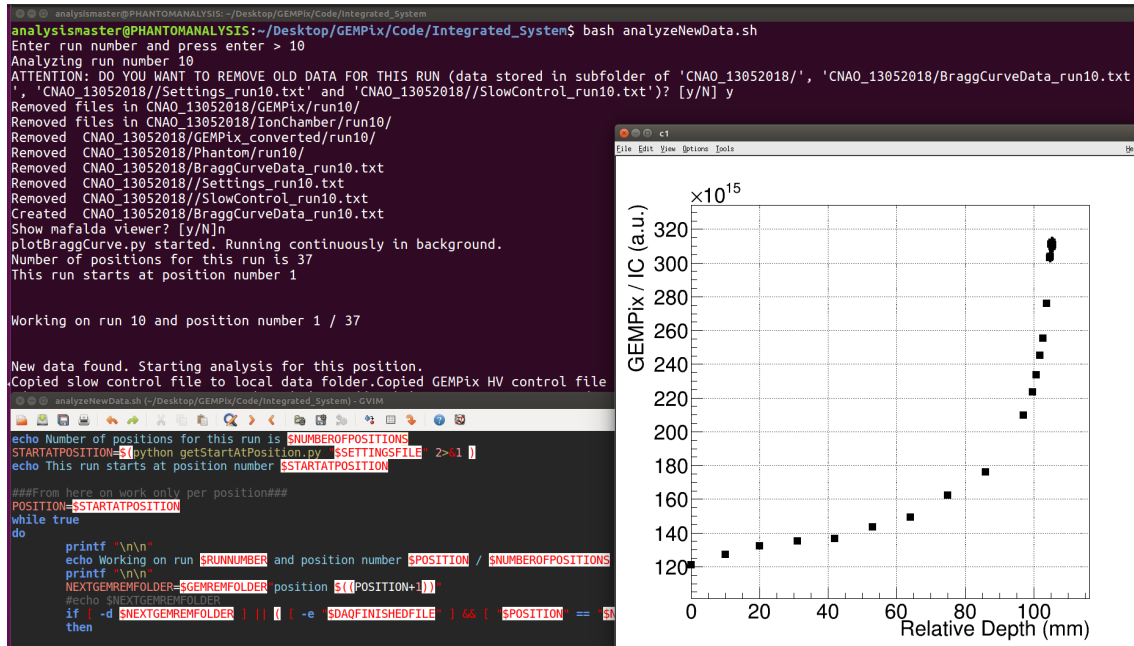


Figure 5.19: Screenshot of the bash script controlling the online analysis (bottom left), the terminal output when analysing a run (top) and the display of the analysed data (right).

5.5.1. Ionisation Chamber at CERN's Calibration Laboratory

CERN's calibration laboratory [165] is located at the Prévessin site and is mainly used for calibration of all CERN radiation monitors (fixed and portables), the personal dosimeters and for tests of radiation hardness of electronics. There are one small room with a very high activity gamma source and a large hall with high activity gamma sources, a neutron source, a beta irradiator and an X-ray generator. For this test, the ^{60}Co source with a nominal activity of 10 TBq in the small room is used. The ionisation chamber is placed on a moving table to vary the distance between source and detector, while the PTC IC101 and the control laptop are placed outside the measurement room. The measurement duration, which is 60 s, is set in the source control system of the calibration laboratory: the source can be moved in and out by a pneumatic system. Figure 5.20 shows the set-up.

Reference dose rate values are obtained by a separate measurement campaign in which the described ionisation chamber for the water phantom is used together with a 1 cm³ Rigid Stem Chamber – PTW 30015 – read out by the PTW Unidos Dosimeter which provides the dose rate. Several measurements with the PTW 34080 ionisation chamber (in the following referred to as runs) are performed at the calibration

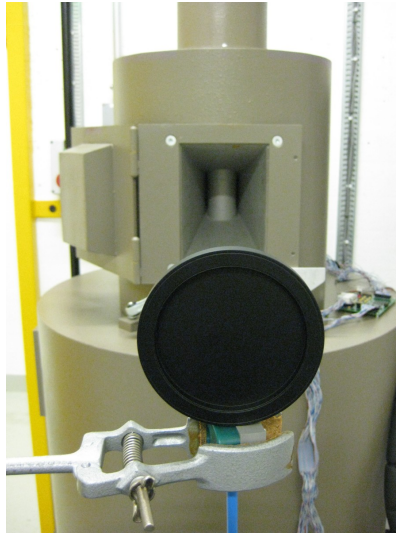


Figure 5.20: The ionisation chamber (foreground) in front of the system containing the radioactive source (background). The small window visible above the ionisation chamber can be opened and the source is placed at the opening by a pneumatic system.

laboratory. Table 5.2 provides a list of all runs and the most relevant settings. The source is not always placed in the very same position by the pneumatic placement system when it is moved out and in again, and differences in the dose rate of a few percent can be assigned to this. Therefore it is noted when the source is moved out and in. Varied settings for the ionisation chamber or the readout are⁽¹³⁾:

- The distance between source and ionisation chamber: compare runs 17 through 21.
- The trigger: external hardware trigger (ext) or internal software trigger (int). Compare runs 2 and 3 and runs 4 and 8.
- The resolution of the measurements: the number of integrations (int) and readings (read) of the charge during the set measurement time are automatically calculated depending on the chosen resolution or vice versa. When the number of integrations or readings is set manually, the numbers are given in the remarks. Compare runs 1 and 2, 3 and 4, 8 through 10.
- The integration time. In some cases (with a high resolution), the integration time depends slightly on the chosen settings, yielding 49.97 ms instead of 50 ms. Compare runs 1, 11 and 12.

⁽¹³⁾ Stated run numbers refer to the runs where only the specific parameter is changed.

- The HV for the ionisation chamber. Compare runs 4 through 7.
- The possible shift to the left or right (seen from the source looking to the ionisation chamber). Compare runs 13 through 16 and 23.
- The possible tilting angle of the ionisation chamber with respect to the direct line between source and detector position. Compare runs 22 and 24.

Table 5.2.: List of all runs performed with the PTW 34080 ionisation chamber at CERN's calibration laboratory.

Run No.	Distance (cm)	Trigger	Resolution (bits)	Integration time (ms)	Set HV (V)	Special Remarks	Measured Current (nA)
1	125	ext	20	49.97	400		0.184
2	125	ext	16	50.00	400		0.185
3	125	int	16	50.00	400		0.185
4	125	int	20	49.97	400		0.184
5	125	int	20	49.97	405		0.184
6	125	int	20	49.97	350		0.184
7	125	int	20	49.97	300		0.184
8	125	ext	20	49.97	400		0.184
9	125	ext	19	50.00	400	manual settings: read. = 1, int. = 10	0.185
10	125	ext	19	50.00	400	manual settings: read. = 2, int. = 5	0.185
11	125	ext	20	100.0	400		0.184
12	125	ext	20	20.00	400		0.185
13	125	int	20	49.97	400	source out after run	0.184
14	125	int	20	49.97	400	ion chamber moved 5 mm to the right as seen from source, source out after run	0.178
15	125	int	20	49.97	400	ion chamber still 5 mm to the right as seen from source, source out after run	0.180
16	125	int	20	49.97	400	ion chamber back to center position, source out after run	0.175
17	124.5	int	20	49.97	400	source out after run	0.177
18	100	int	20	49.97	400	source out after run	0.289
19	80	int	20	49.97	400	source out after run	0.485

Table 5.2.: List of all runs performed with the PTW 34080 ionisation chamber at CERN's calibration laboratory (continued).

Run No.	Distance (cm)	Trigger	Resolution (bits)	Integration time (ms)	Set HV (V)	Special Remarks	Measured Current (nA)
20	60	int	20	49.97	400	source out after run	1.035
21	50	int	20	49.97	400	source out after run	1.577
22	125	int	20	49.97	400	chamber rotated by $\approx 45^\circ$ about vertical axis, source out after run	0.188
23	125	int	20	49.97	400	no tilt, chamber moved 4 cm to the right as seen from source, source out after run	0.174
24	125	int	20	49.97	400	chamber centered, rotated by 90° about vertical axis, source out after run	0.139

Figure 5.21 shows the results of one run as a histogram containing all single current measurements. At the calibration laboratory the noise is typically contained in (0 ± 5) fA, while a current during irradiation of about 200 pA or more is measured. The temperature and pressure correction (see equation 5.1) is applied; mean, sigma and the corresponding uncertainties are obtained by fitting a Gaussian function to this distribution.

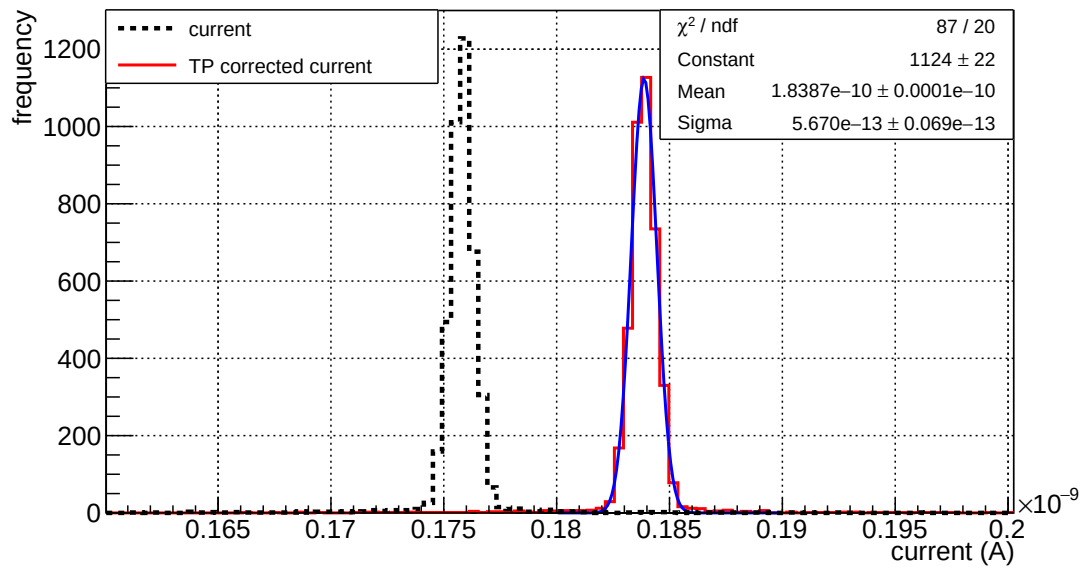


Figure 5.21: Histogram of the current measurements with one setting (run 1, see table 5.2). Uncorrected (black dashed line) and temperature and pressure corrected (red solid line) distributions are shown. A Gaussian fit to the corrected distribution gives the mean current value of the measurement, in this case 184 pA.

Figure 5.22 shows the measured mean values of the current for all runs, except when the distance and thus dose rate are changed (i.e. runs 18 through 21 are excluded). Changes in the source dose rate of a few percent are possible when the source is moved out and in again; the source is moved out for the first time after run 13. Except for the last run (when the ionisation chamber is rotated by 90°) the changes in the dose rate are most likely explained by this effect. As expected, none of the changed settings has a major impact on the current measurement. Figure 5.23 shows the measured resolution for all runs. In runs 2 and 3, a larger value is observed since the resolution of the readout is decreased. In run 11 the integration time is larger which leads to smaller fluctuations while the opposite is true for run 12. Larger currents are measured with smaller relative fluctuations as observed in runs 18 to 21.

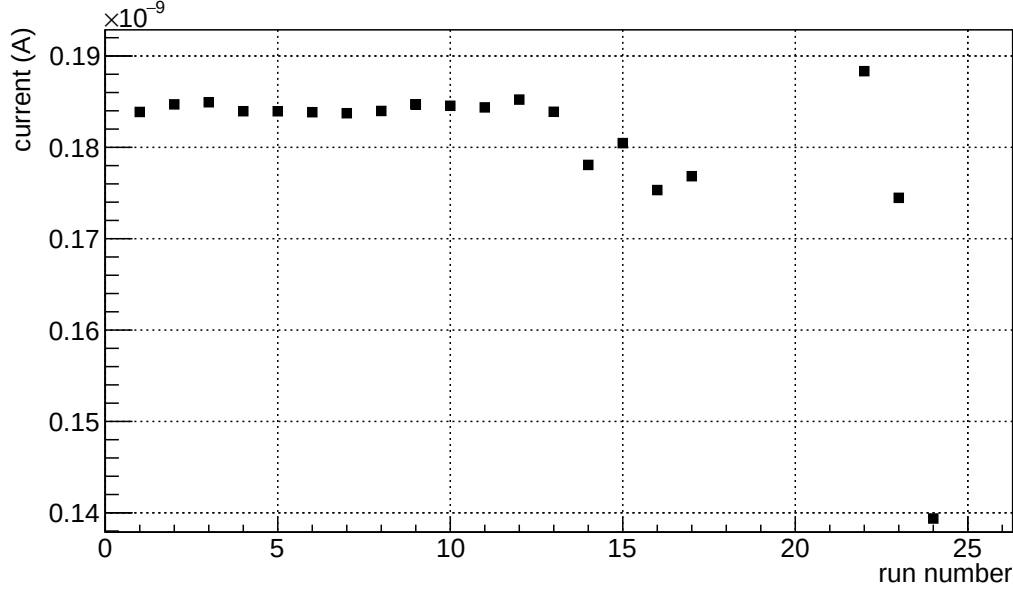


Figure 5.22: Current measured in the different runs at the calibration laboratory. Uncertainty bars are smaller than the data points.

The mean values and their uncertainties are then used to produce the linearity plot (figure 5.24). The current is plotted against the dose rate at each measurement position, which is obtained from the reference measurements. The slope of the linear fit applied to the data is converted into the detector response:

$$\text{response (nC/Gy)} = \text{slope (A/(Gy/h))} \cdot 3600. \quad (5.2)$$

The calculated ionisation chamber response of $(328 \pm 3) \text{ nC/Gy}$ fits well the nominal response of 325 nC/Gy , as shown in figure 5.24. All tests at the calibration laboratory demonstrated that the ionisation chamber and its readout perform as stated in their specifications. A similar test is also performed with a ^{137}Cs source at the calibration laboratory as an independent test. These results are presented in the appendix (section A.8).

5.5.2. Ionisation Chamber at CNAO

Set-up

The test that is closest to the application as a reference chamber for the integrated system – and thus most important – is the test in beam. At CNAO, proton and

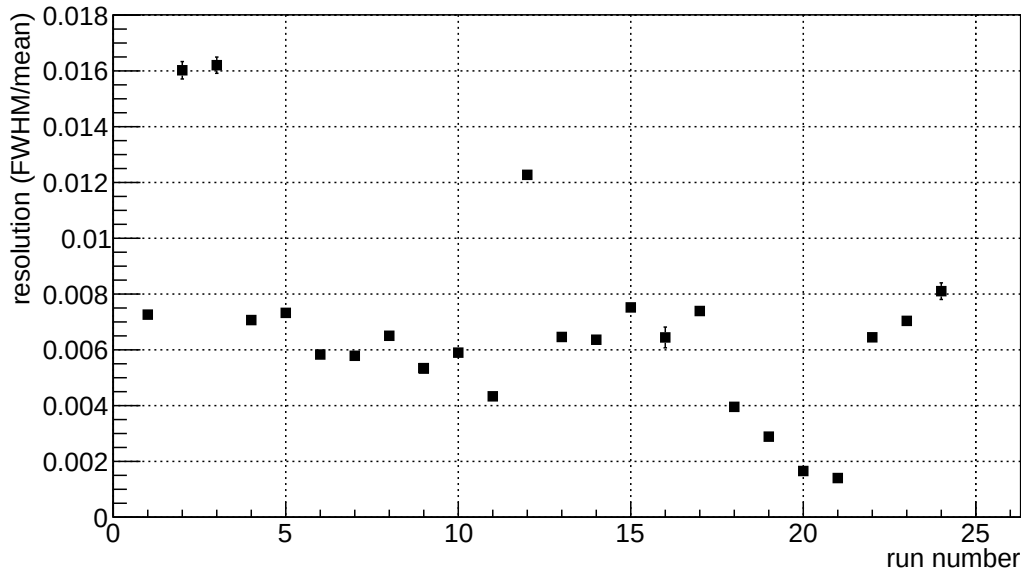


Figure 5.23: Resolution (FWHM divided by the mean value) measured for all runs. Uncertainty bars are often smaller than the data points.

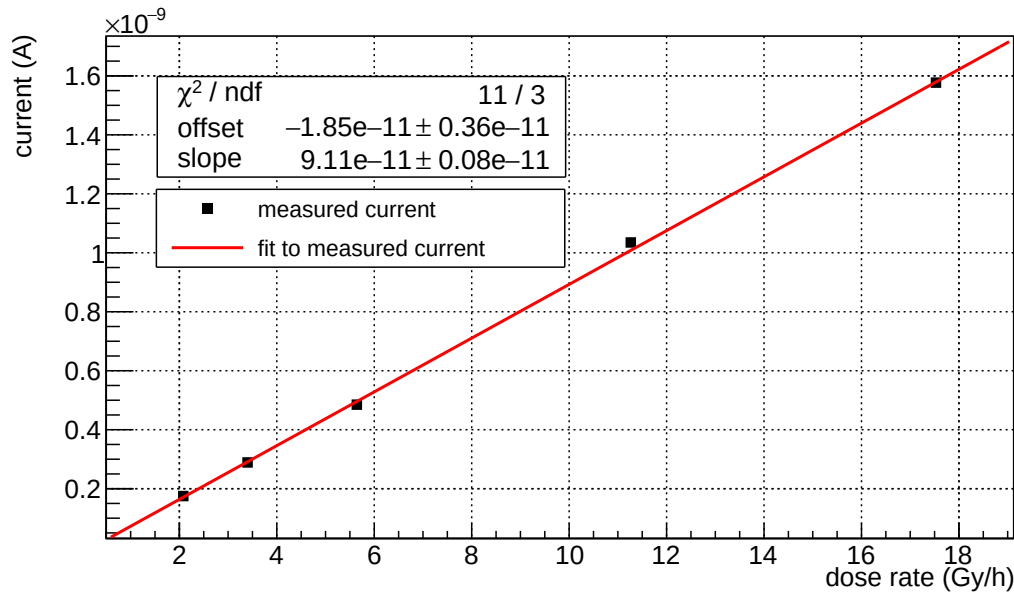


Figure 5.24: Linearity check with the ionisation chamber at the calibration laboratory. The chamber response is quite linear and from the slope of the fit the response is calculated as $(328 \pm 3) \text{ nC/Gy}$.

carbon ions are used with many different settings to check the performance of the ionisation chamber.

Figure 5.25 shows the set-up: the PTW ionisation chamber is put directly in the beam and the PTC IC101 is used as readout and to supply the HV of 400 V. Every 50 ms a measurement with an integration time of 50 ms is started. For comparison, data from the DDS are also obtained. The DDS readout is event driven but usually provides a value every 50 ms.

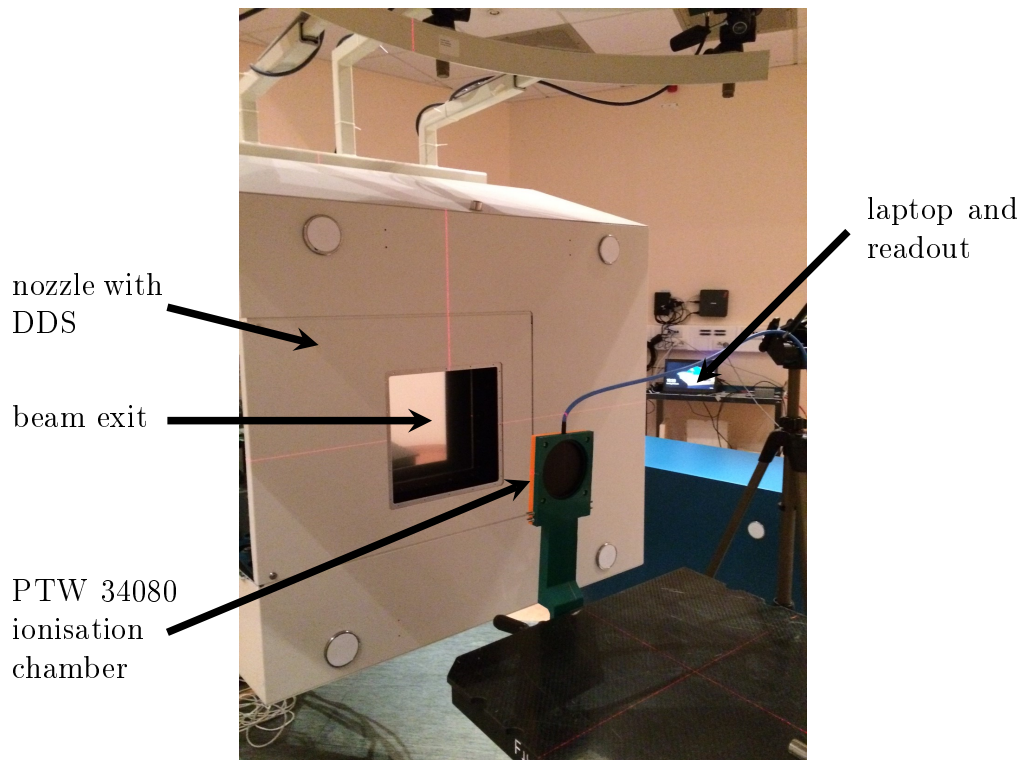


Figure 5.25: The ionisation chamber is set up in front of the beam nozzle in treatment room 3 at CNAO.

Measurements

The measurements include five different beam energies, different degrader settings, relocating the beam spot and using a scanned field. Measurements are performed with carbon ions as well as protons. Data obtained from the DDS consist of a relative time stamp starting from 0 for each run and measured counts from the two DDS detectors. Data obtained from the PTW ionisation chamber consist of an absolute time stamp, the measured current and the number of triggers received. Table 5.3

provides the detailed settings for all runs. Table 5.4 states the nominal size of the beam at the isocentre for the used energies. There is no significant deviation from these values expected at the position of the PTW ionisation chamber for carbon ions, while the beam size is expected to be 10 to 15% smaller at this position for protons.

Table 5.3.: List of all runs performed with the PTW 34080 ionisation chamber at CNAO.

Run No	Particle	Range (mm H ₂ O)	Energy (MeV/u)	Remarks on beam settings
1	C	50	151	
2	C	50	151	
3	C	150	280	Energy scan: affects energy, beam diameter, and instantaneous intensity
4	C	250	380	
5	C	200	332	
6	C	100	222	
7	C	100	222	Auto. degrader: 50%
8	C	100	222	Auto. degrader: 20%
9	C	100	222	Man. degrader: 20%
10	C	100	222	Man. degrader: 50%
11	C	100	222	Beam spot at (1 cm, 1 cm)
12	C	100	222	Beam spot at (−1 cm, −1 cm)
13	C	100	222	Beam spot at (2 cm, 2 cm)
14	p	101	118	Energy scan: affects energy, beam diameter, and instantaneous intensity
15	p	201	174	
16	p	320	227	
17	p	101	118	Auto. degrader: 50%
18	p	101	118	Auto. degrader: 20%
19	p	101	118	Man. degrader: 50%
20	p	101	118	Beam spot at (1 cm, 1 cm)
21	p	101	118	Beam spot at (−1 cm, −1 cm)
22	p	101	118	Beam spot at (−2 cm, −2 cm)

Table 5.4.: Beam sizes for different beam energies at CNAO [166].

Particle	Range (mm H ₂ O)	Beam size in x (FWHM in cm)	Beam size in y (FWHM in cm)
proton	50	1.51	1.71
proton	101	1.13	1.21
proton	151	0.97	1.01
proton	201	0.88	0.87

Table 5.4.: Beam sizes for different beam energies at CNAO [166] (continued).

Particle	Range (mm H ₂ O)	Beam size in x (FWHM in cm)	Beam size in y (FWHM in cm)
proton	250	0.81	0.80
proton	320	0.73	0.75
C	50	0.64	0.72
C	100	0.53	0.57
C	150	0.50	0.46
C	200	0.404	0.461
C	250	0.392	0.513

Analysis of a Single Run: Run 1

In the following paragraphs, the analysis of the data of a single run is explained using run 1 as an example. Analysis of other runs is performed in the same way and similar results are obtained. The main difference is the instantaneous beam intensity and the spill structure that changes especially due to the degraders. Figures 5.26 and 5.27 show the raw data of the PTW ionisation chamber and the DDS, respectively, for run 1. A relative time stamp starting at 0 for this run is introduced for the PTW ionisation chamber data. A correction factor between the two DDS detectors has to be applied [167], and the uncertainty on this factor is obtained as the sigma of a Gaussian fit, in this case estimated to be 0.2%. This parameter is used in the next section and in the appendix (section A.9) to obtain an uncertainty on the DDS values. In the appendix, figure A.8 compares the two DDS detectors in terms of the ratio of the measurements.

Since the DDS and the PTW ionisation chamber do not measure synchronously and the DDS does not provide an absolute time stamp, a time shift that is different for each run has to be found as for the measurements with the CNAO water phantom (section 5.3). It is systematically adjusted as explained later.

In general, the PTC IC101 readout integrates the charge on a capacitor for a given integration time. Then it discharges the capacitor and starts a new measurement. Different techniques are implemented to increase resolution: there is a read and an integration average that both affect data taking. If the read average is set to a number of readings n , it means that the charge on the capacitor is read out n times and the average of these readings is calculated. The effect on the data taking in terms of time resolution is expected to be rather small since only the dead time is affected but it is of the order of 10 μ s to 100 μ s. Unfortunately, the effect of the integration averaging is larger, a fact that is noticed only after data taking at CNAO. If the

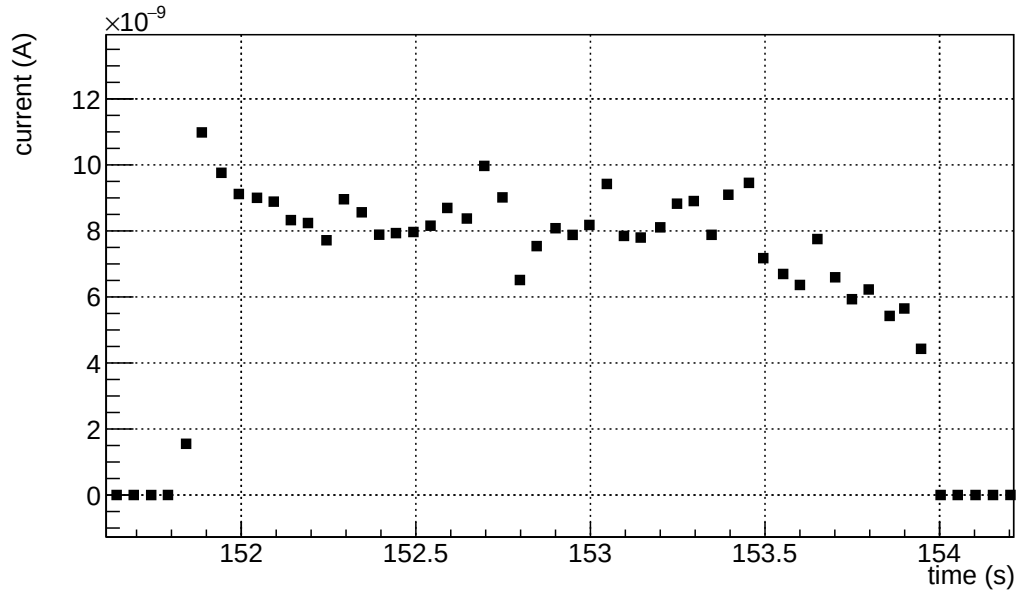


Figure 5.26: Raw data of the PTW ionisation chamber for run 1, zoomed to one spill. The measured current during a spill plateau is typically in the order of 5 nA to 17 nA. Smaller values are observed on the rising and falling edge.

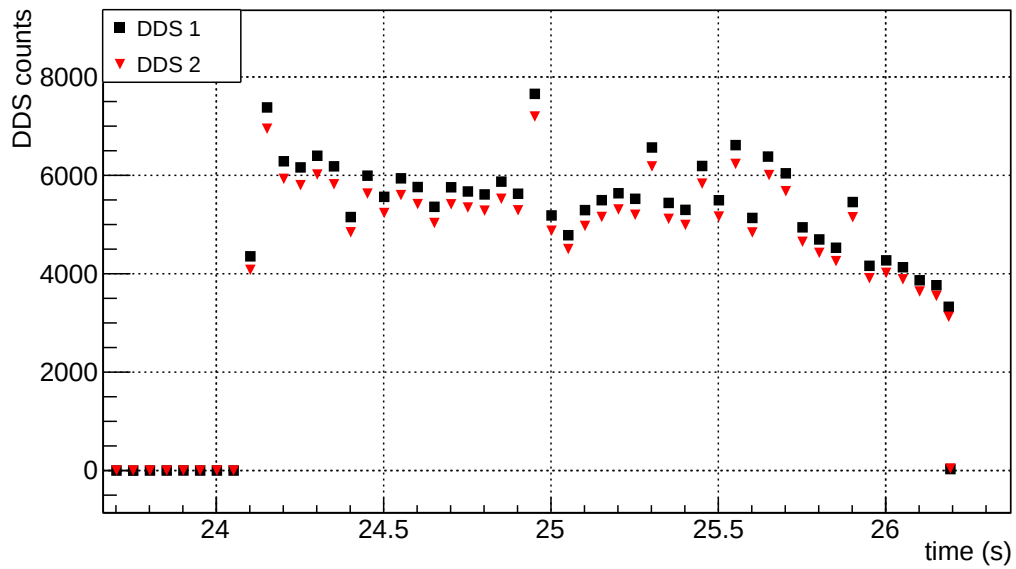


Figure 5.27: Raw data of the two DDS detectors for run 1, zoomed to one spill. Eleven spills are measured (typically around ten per run). Typical DDS counts during spill are between 3000 and 12000.

integration average is set to n , it means that the average of the last n measurements of the set integration time is calculated. This effect leads to smearing in the data taken at CNAO, since the integration average is set to 2 for all measurements at CNAO. However, it is possible to reverse this smearing by an algorithm, as the total number of data points remains the same. This is explained in more details in the appendix section A.9. In the following, only results using this algorithm are presented.

Figure 5.28 compares the current measured by the PTW ionisation chamber and the counts of the DDS 1 for run 1. Current values of the PTW ionisation chamber are multiplied by a normalisation factor and DDS 1 counts are scaled for visualisation only by the mean scaling factor of all runs that is calculated later. A linear interpolation between successive DDS data points is introduced and the interpolated value at the time of each data point of the PTW ionisation chamber is calculated. This technique improves the comparability of the DDS and the PTW ionisation chamber measurements. Usually the DDS takes data every 50 ms, which should also be the case for the PTW ionisation chamber. However, it is noticed that this assumption does not hold and differences of up to some 10 ms are observed. These outliers are much larger than the expected and observed Gaussian distribution and are most probably due to the LabVIEW data acquisition software. Note that for measurements with the integrated system, a stabler external trigger system is used. For the data presented here a simple cut on the time between two successive current measurements improves data quality: only data points that are (50 ± 3) ms after the previous measurement are taken into account.

Two more cuts are applied for further analysis: data points with less than 1000 interpolated DDS counts are excluded to compare only values during spill. It is also required that two successive current measurements of the PTW ionisation chamber differ by no more than 20%. This cut excludes values at the very beginning and at the very end of a spill. It is checked that this cut removes roughly two values per spill for all runs as expected and is not excluding values during spill.

In order to find the correct time shift, the interpolated DDS 1 counts are plotted versus the current measurements of the PTW ionisation chamber (figure 5.29). Uncertainties of 1% on the current measurements are applied. This number is justified by the data provided by the manufacturers of the ionisation chamber and readout and by the measurements at the calibration laboratory: table A.4 in the appendix states the uncertainties for the ionisation chamber which are given as maximum values. From the measurements at the calibration laboratory the uncertainty appears to be less than 1%. The readout adds another 0.5% uncertainty at maximum. In total, an uncertainty of 1% is applied. Uncertainties on the interpolated DDS counts are obtained from error propagation on the linear interpolation: a 0.3% uncertainty

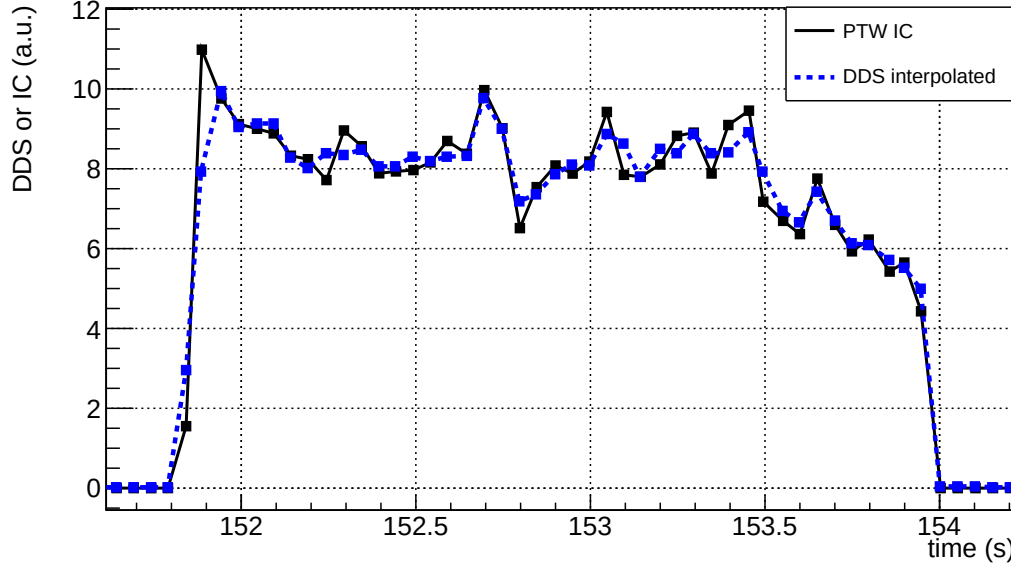


Figure 5.28: Scaled and time shifted values for the same spill of run 1 as in figures 5.26 and 5.27. A straight line between successive data points is drawn for better visualisation. Statistical fluctuations between DDS 1 and PTW ionisation chamber measurements are visible.

is applied on the raw DDS counts in general and a 0.1ms uncertainty is applied on the time of the PTW ionisation chamber data points. A linear relation between DDS counts and PTW ionisation chamber current is expected but the fit quality is not satisfactory within the applied uncertainties. However, no systematic trend is observed. Uncertainties for the comparison between DDS and PTW ionisation chamber are further discussed in the next section.

Although the fit quality is not satisfactory, this fit is used for an automatic search for the time shift between DDS and PTW ionisation chamber. The value that is found as a first guess is used as a starting point and is varied plus and minus 20 ms in steps of 1 ms. Therefore the plot as in figure 5.29 is obtained 41 times per run. The time shift with the smallest χ^2/NDF is chosen for the following analysis.

In order to better quantify the deviations from the linear relation, the ratio of DDS 1 counts to current measured by the PTW ionisation chamber is investigated in a histogram (figure 5.30). The mean value of a Gaussian fit equals one due to the applied scaling. The fluctuations of the ratio indeed follow a Gaussian distribution with a sigma of 4.0%. The meaning of this is better discussed in the next section.

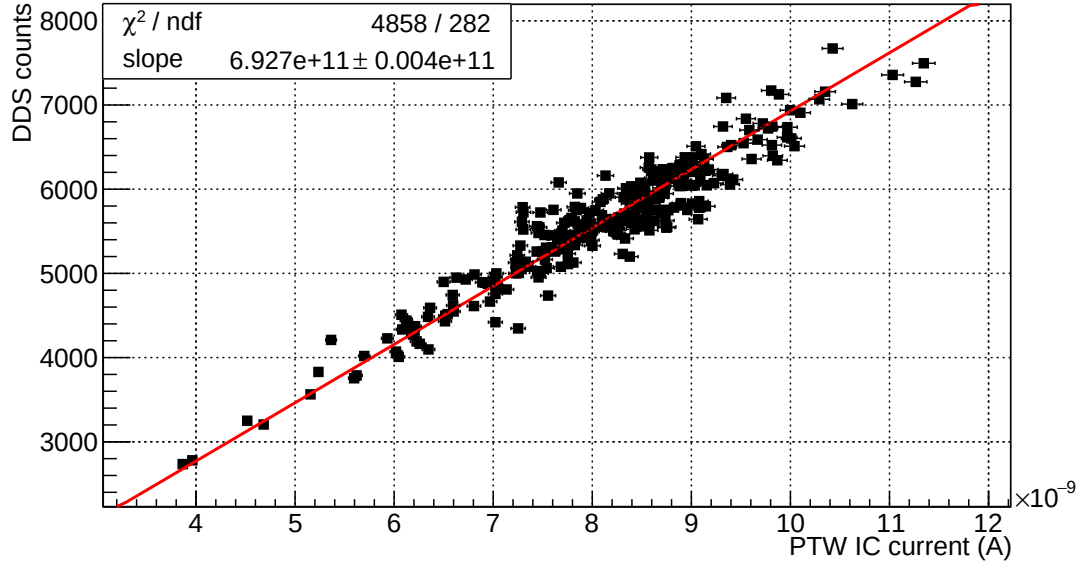


Figure 5.29: The quality of the linear fit to DDS 1 counts versus PTW ionisation chamber is not satisfactory, but no systematic trend is observed. The offset is fixed to be zero.

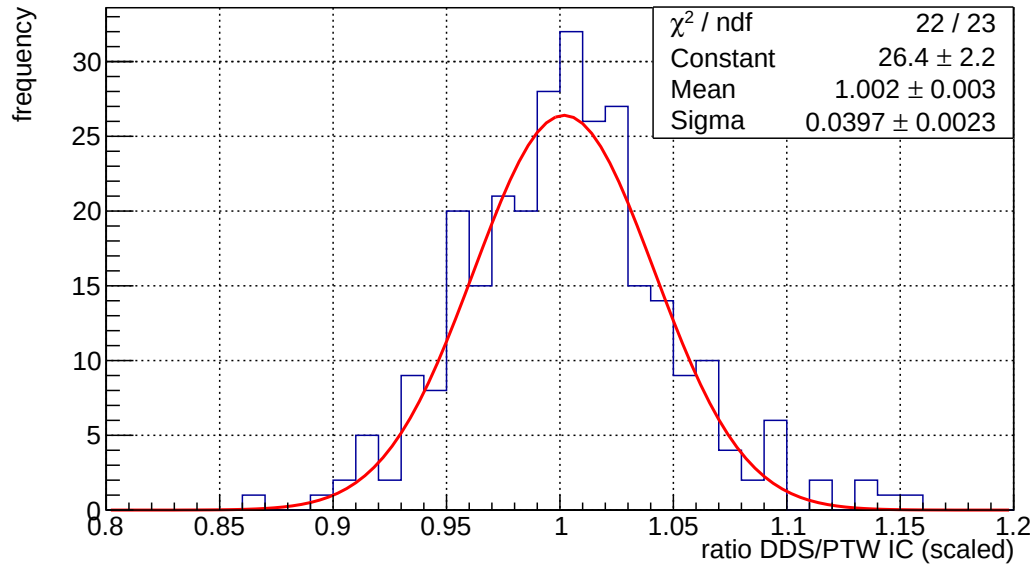


Figure 5.30: The ratio of the DDS 1 counts and the PTW ionisation chamber current for run 1 equals 1 on average due to the scaling. A sigma of 4.0% is obtained.

Comparison of Runs and Uncertainty Treatment

In this section, results from the analysis of single runs are compared and the treatment of uncertainties is discussed in more details. Figure 5.31 compares the sigma of the Gaussian fit to the distribution of the ratio of DDS 1 counts to PTW ionisation chamber current for all runs. The values are within 2% to 6.5% and give an estimate of the uncertainty on a single 50 ms measurement with the PTW ionisation chamber. All three cuts explained in the previous section are applied.

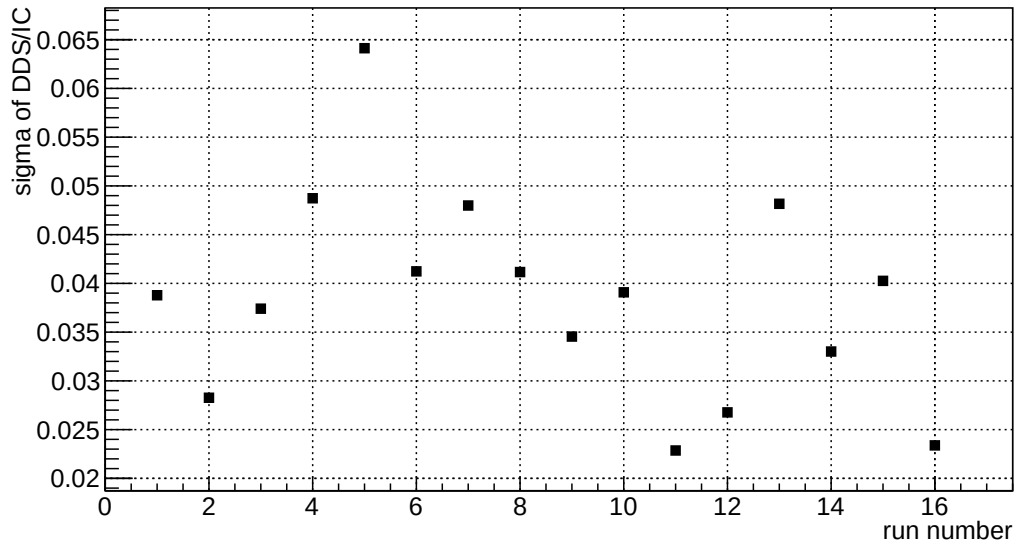


Figure 5.31: The values for sigma of the Gaussian fits to the ratio of DDS 1 counts and current of the PTW ionisation chamber, as shown for run 1 in figure 5.30. No systematic dependence on the run settings is noticed.

When performing depth scans with the integrated system, more than one value per position is measured. Therefore the application of the PTW ionisation chamber as a reference detector for measurements with the GEMPix is mimicked: only one value every 6 is taken into account during spill and again all three cuts mentioned in the previous section are applied. This results in one measurement every 300 ms, which is approximately comparable to the maximum dead time of the GEMPix. The sum does not include the whole run but is stopped at 20 values, which is approximately equal to the number of measurements per position in a depth scan with the GEMPix. This method produces maximum fluctuations within $\pm 2\%$. On average, the ratio of DDS 1 to the ionisation chamber is 685.5 counts/nA with a relative uncertainty of 1.34%.

5.5.3. Conclusions of the Test Measurements

The performed tests prove that the PTW ionisation chamber together with the PTC IC101 readout can be used as a reference detector for measurements with the GEMPix in a water phantom. An uncertainty of 1 to 1.3% is expected e.g. depending on the number of measurements per position. This uncertainty is to be understood in the sense of a comparison between DDS and PTW ionisation chamber. No systematic dependence on the beam settings such as the beam energy is noticed. The tests with the ^{60}Co source at the Calibration Laboratory confirm the nominal response to the radiation dose rate and the response is well linear.

5.6. FLUKA Simulation

The final simulation of the integrated system with the Monte Carlo simulation software FLUKA (see section 2.4.5) is carefully motivated by looking first at measurements and simpler simulation set-ups:

- Data of measurements at CNAO with the PTW peakfinder (see section 5.1.7) are provided by Mario Ciocca (CNAO). The peakfinder measures the ratio between an ionisation chamber at a certain depth in water and a reference detector in front of the set-up. Depths are chosen to cover the full Bragg curve and smaller spacing around the Bragg peak ensures good resolution.
- The simulation called here ‘CNAO reference simulation’ contains the full acceleration and beam delivery complex and a very simple set-up in the treatment room: a block of water surrounded by air. The dose in water is scored in slices of $50 \times 50 \text{ cm}^2$ at different depths. Simulation results are provided by Andrea Mairani (CNAO and HIT).
- The simulation called here ‘CERN large area’ uses the phase space files provided by Andrea Mairani (see section 5.6.1) and also contains only the block of water surrounded by air in the treatment room. The dose is scored in slices of $50 \times 50 \text{ cm}^2$ in depth bins of 0.1 mm thickness from 0 mm to 300 mm. For the results presented here, ten simulation runs each with 100,000 primary particles are combined. The computing time on a single core is about 8 h in total.
- The simulation called here ‘CERN small area’ has exactly the same set-up and settings as the ‘CERN large area’ simulation but depth bins only have an area of $2.82 \times 2.82 \text{ cm}^2$ (the same size as the GEMPix sensitive area).

- The simulation of the integrated system (‘CERN integrated system’) uses the same phase space files as the other CERN simulations but the geometry of the integrated system. See section 5.6.2 for more details.

Uncertainty values for the peakfinder measurements and the CNAO reference simulation are not available. However, typical statistical uncertainties are less than 1%. For the CERN simulations, statistical uncertainties are calculated based on the variance of the repeated runs that are combined for the final result. They are less than 1% for all CERN simulations.

In the following the simulation for carbon ions with a range of 150 mm and usage of two ripple filters is explained in detail, similar results are obtained for other energies. Step-by-step comparison of the measurements and simulations is shown in sections 5.6.3 to 5.6.6. To present these plots in a consistent manner, uncertainties are not plotted even when available but they are for all measurements and simulations less than 1% – as described above.

5.6.1. Phase Space Files

All CERN simulations start in air at the exit of the beam off the nozzle with particle distributions generated by Andrea Mairani (CNAO and HIT) in the standard CNAO simulation set-up: the full accelerator chain is simulated and the particles are scored at the beam exit. The main properties written to so-called phase space files are the particle type (mass and atomic number), the energy, x and y position, x and y direction of propagation⁽¹⁴⁾. Each phase space file contains information of a simulation with one million primary carbon ions. Figure 5.32 shows the kinetic energy distribution of the carbon ions and figure 5.33 the positions of the carbon ions⁽¹⁵⁾.

5.6.2. Implementation of the Integrated System in FLUKA

Figure 5.34 shows the implemented geometry of the integrated system. The goal is to implement carefully the full geometry in the beam path (including the expected spread-out) while simplifying the parts outside the beam path. The water phantom box, the water, the GEMPix box, the GEMPix and surrounding air are included and only somewhat simplified in case of the GEMPix. An example for a part that is left out is the holder of the GEMPix box.

⁽¹⁴⁾This is sufficient spatial information as all particles are scored in the same plane.

⁽¹⁵⁾The distributions of the x and y projections can be found in the appendix in figure A.10.

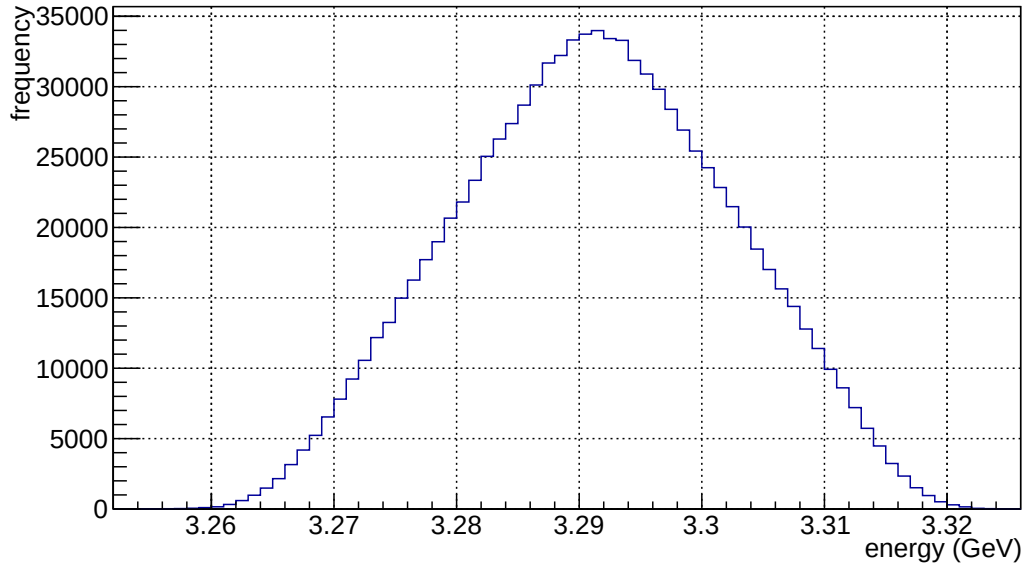


Figure 5.32: The kinetic energy distribution of the carbon ions leaving the beam nozzle.

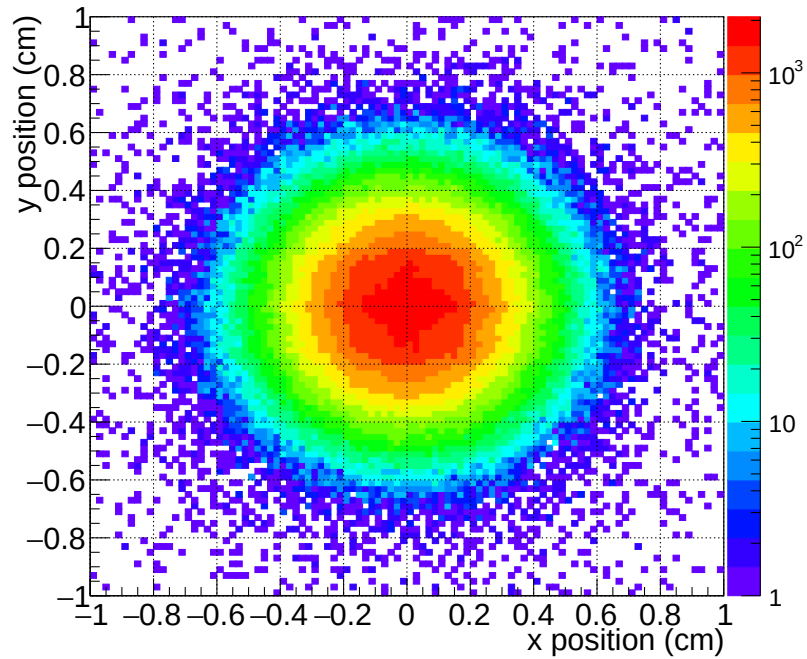


Figure 5.33: The position of the carbon ions when leaving the beam nozzle. The frequency is colour coded in logarithmic scale.

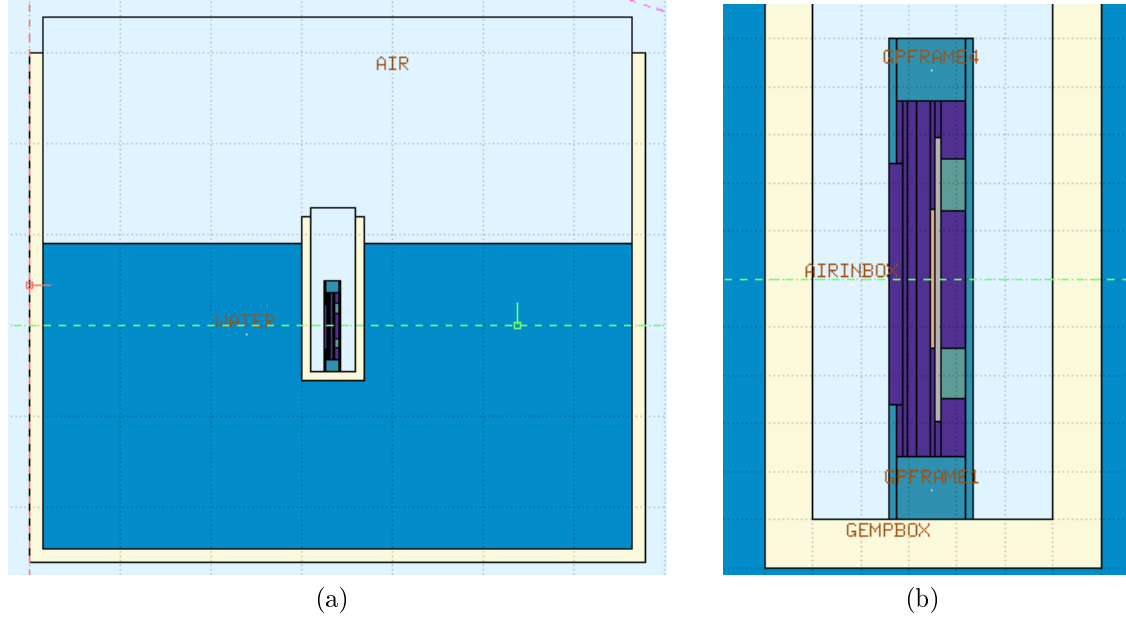


Figure 5.34: (a) the implemented water phantom and (b) a zoom to the GEMPix in FLUKA.

The depth scan procedure needs to be implemented since a continuous depth binning as for the other simulations is not possible – the box with the GEMPix must be shifted in depth. The depth shift is implemented as a single variable which simplifies the procedure in FLUKA: a loop over this one variable creates a run for each depth scan. This is also useful with respect to the run time, since for each depth the same number of primary particles as for the full depth scan for the other CERN simulations is needed. Runs can be easily distributed to different cores, thus decreasing the computing time. Typically simulations are distributed to the four cores of a laptop with results ready overnight. If needed in the future, this structure can be made very easily ready for distribution on more cores, i.e. a computing cluster.

5.6.3. CNAO Reference Simulation Compared to Peakfinder Measurements

In a first step, measurements with the PTW Peakfinder are compared to the CNAO reference simulation. Figure 5.35 shows that there are significant differences between the two data sets mainly due to the different sensitive areas: the peakfinder uses an ionisation chamber with a diameter of approximately 8 cm while in the FLUKA simulation a scoring area of $50 \times 50 \text{ cm}^2$ is used. When the beam size increases due

to scattering and production of secondary particles, the differences become up to 20%, as seen in the tail. Note that for quality assurance measurements at CNAO a correction is implemented and experimental and simulated results match well (as shown in figure 2.4 in chapter 2).

5.6.4. CERN Large Area Simulation Compared to CNAO Reference Simulation

In order to check the correct use of the phase space files and reduce possible error sources to the implemented geometry, the simple geometry is tested to match the CNAO reference simulation within $\pm 1\%$ (figure 5.36). Anything but a good match would be surprising as the same set-up is used but this comparison serves as the basic check before the rather complicated geometry of the integrated system is implemented.

5.6.5. CERN Small Area Simulation Compared to CERN Large Area Simulation

In another preparatory step, two CERN simulations with exactly the same set-up but different area of the scoring slices are compared. The larger ones have an area of $50 \times 50 \text{ cm}^2$ while the smaller ones have the same area as the sensitive area of the GEMPix ($2.82 \times 2.82 \text{ cm}^2$). This step disentangles effects only due to the relatively small sensitive area of the GEMPix and effects due to the used materials such as the detection gas. Figure 5.37 shows that the size of the area has a significant effect especially in the tail of the Bragg curve.

5.6.6. CERN Integrated System Simulation Compared to CERN Small Area Simulation

The last step is the comparison of the small area simulation to the final simulation of the integrated system. Figure 5.38 shows only small differences between the two set-ups for plateau and Bragg peak ($\pm 2\%$) and a small change by approximately 5% in the tail. The chosen material and the stopping power of the gas apparently have a rather limited effect on the deposited energy. Note that also in the simulation of the integrated system, no signal processing is implemented. Only the deposited energy in the sensitive volume is simulated but neither the gas amplification nor the Timepix signal detection are considered here.

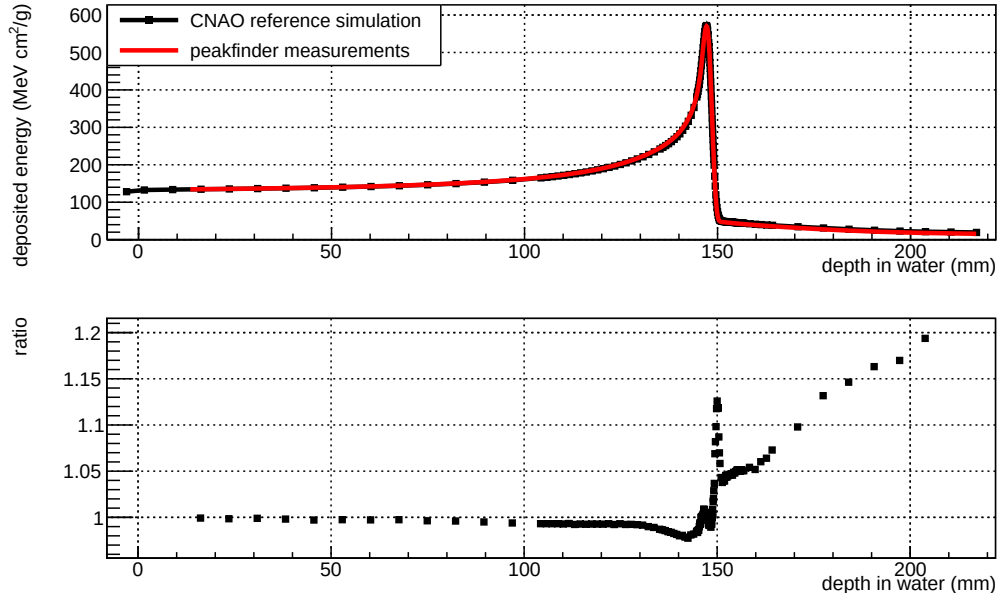


Figure 5.35: The Bragg curves obtained by a measurement with the PTW peakfinder and by the standard CNAO simulation (upper plot). The ratio reveals significant differences due to the different area (see text for further explanations).

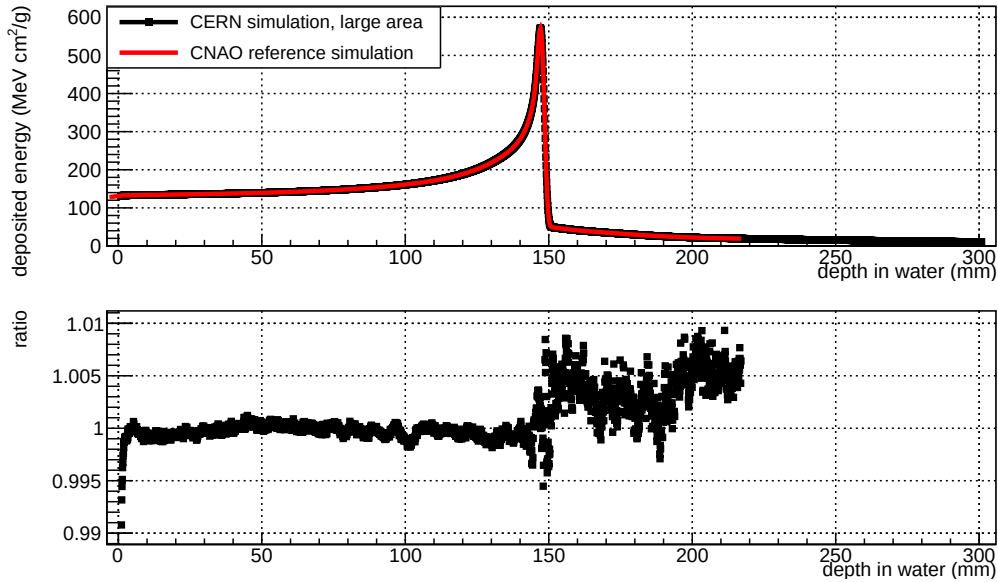


Figure 5.36: The CNAO reference simulation and the CERN large area simulation match well, as expected due to the same set-up.

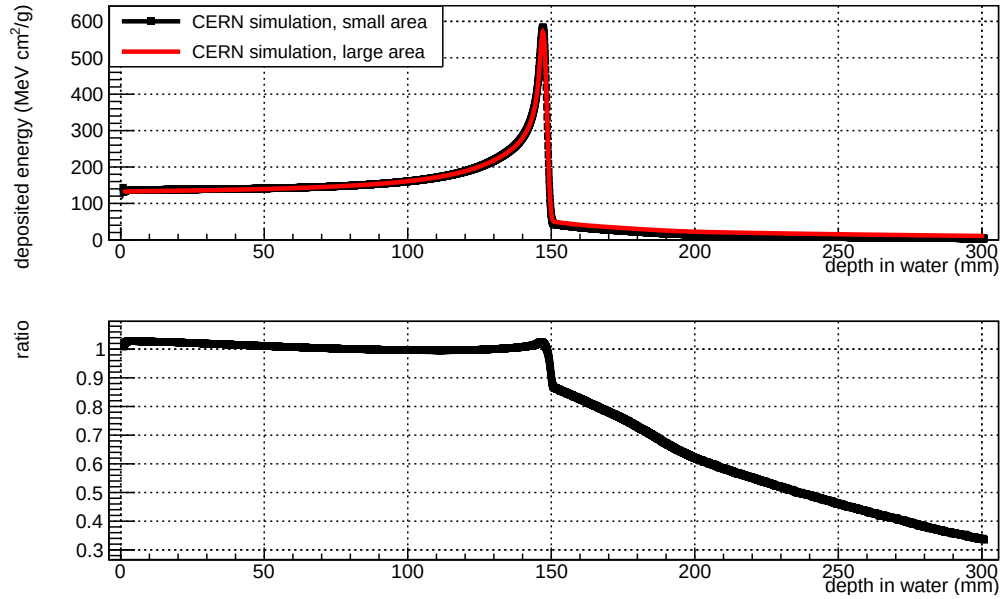


Figure 5.37: The effect of the small sensitive area is largest in the tail of the Bragg curve as the beam is spread out with increasing depth in water.

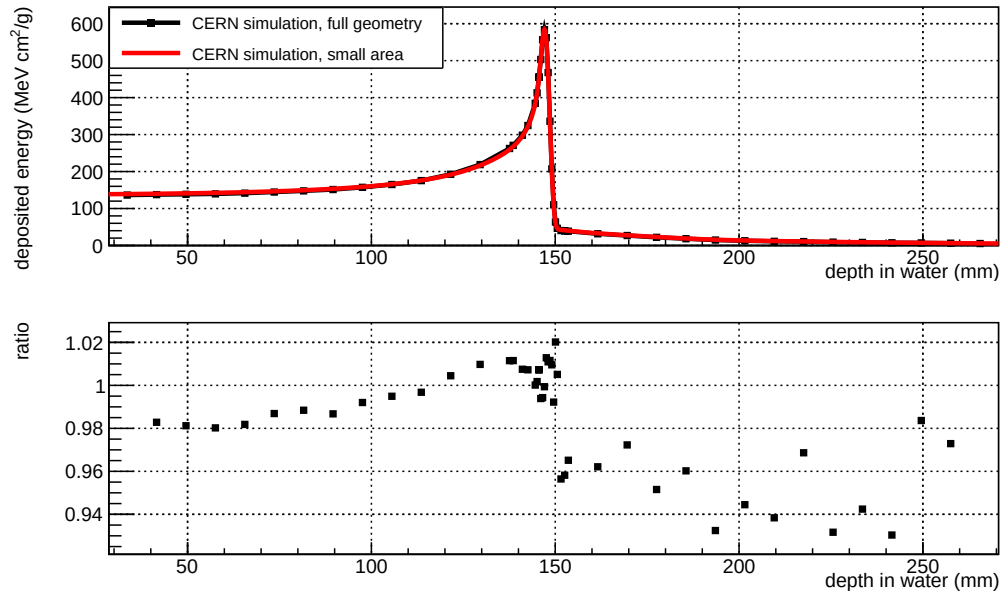


Figure 5.38: Only small differences are observed when comparing the simulation of the integrated system with the small area simulation.

5.7. Measurements at CNAO

Measurements with the integrated system are performed during four shifts at CNAO in the period of September 2017 to May 2018. Table A.7 in the appendix provides a list of the runs at CNAO, selecting only the completed depth scans and meaningful tests but excluding for example aborted runs due to obviously bad settings. The first digit of the run number is the number of the shift, for example run 301 is the first run of the third shift. All measurements with carbon ions are performed with two ripple filters, while the measurements with protons are performed without any ripple filter. The table also provides the beam and GEMPix settings. In the following, only results of selected runs are presented. If not stated otherwise, the simulation of Bragg curves shown for comparison is the final one including the geometry of the integrated system, called ‘CERN integrated system’ (see section 5.6.2).

5.7.1. Depth Scan and Bragg Curve

As for the system based on the CNAO water phantom, the GEMPix measures the energy deposition in several frames at different positions. The data acquisition is described in section 5.4.2. Each frame produces a 2D image as shown for the set-up using the CNAO water phantom in figure 5.9. Compared to the online analysis presented in section 5.4.3 the analysis is extended and includes: the normalisation to the reference measurements with the ionisation chamber; the temperature/pressure correction for the ionisation chamber; the temperature, pressure and humidity correction for the GEMPix data; a normalisation factor for each run to match the FLUKA simulation (which gives results as deposited energy in $\text{MeV cm}^2/\text{g}$).

Figure 5.39 shows the raw data of run 306/307 (carbon ions with 150 mm range in water) compared to the simulation. The measured Bragg curve is very smooth and has small statistical uncertainties of about 2%. An estimated uncertainty of 50 μm is applied on the depth measurement. However, the data do not match the simulation. A similar result is obtained for protons, as shown in figure 5.40 but the mismatch is larger than for carbon ions. In contrast to the measurements with carbon ions, no good GEMPix settings have been achieved yet. The Timepix threshold is believed to be the dominant effect, which increases strongly the peak-to-plateau ratio of the Bragg curve (i.e. the threshold effect is strongest for smaller signals in the plateau). Furthermore, no FLUKA simulation of the integrated system for a proton beam has been performed yet. Therefore, the following analysis is only performed for measurements with carbon ions.

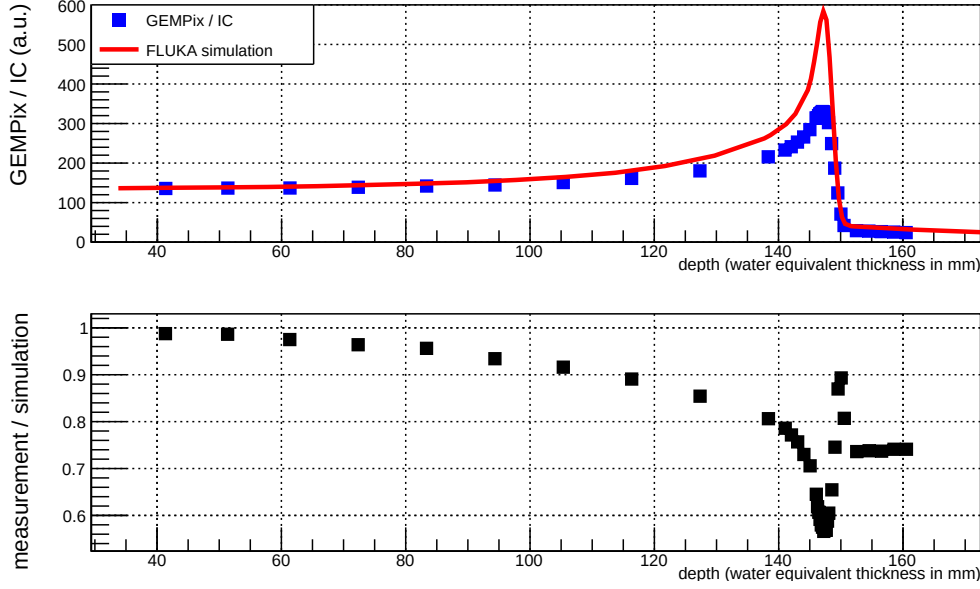


Figure 5.39: Uncorrected Bragg curve data (upper plot) of run 306/307 (carbon ions with 150 mm range) compared to the simulation. The data show a smooth Bragg curve but do not match the simulation, as shown in the ratio (lower plot). Uncertainties are smaller than data points.

5.7.2. Repeated Run as Reproducibility Check

In order to check if the data are reproducible within the assigned statistical uncertainties, a depth scan is repeated and the two results are compared. Figure 5.41 shows the results of runs 109/110 and 114/115. The results are compatible within their statistical uncertainties. This is only a comparison of depth scans of the same shift and therefore systematic differences for example due to a slightly different set-up are not excluded. Nevertheless, the results clearly show that the huge difference between measurements and simulation are not due to largely underestimated statistical uncertainties.

5.7.3. GEM Current Measurements

An analysis of the currents driven by the HV supply for the GEM fields is helpful to disentangle effects in the electron multiplication stage and the Timepix readout. The signal in the GEMs that is expected to be closest to the simulation is the current driven by the induction field (the field between the last GEM and the Timepix readout). The current is measured every second with an estimated integration time of 1 s.

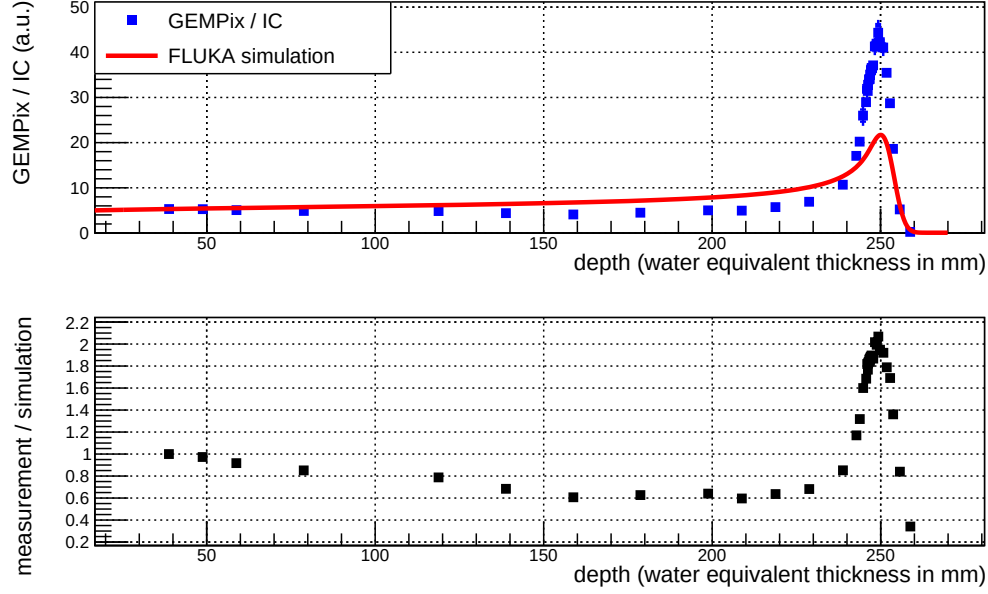


Figure 5.40: Uncorrected Bragg curve data (upper plot) of run 119/120 (protons with 250 mm range) compared to the CNAO reference simulation. The data show a smooth Bragg curve but do not match the simulation, as shown in the ratio (lower plot). Uncertainties are smaller than data points.

No triggering is available and therefore the reference measurement with the ionisation chamber is troublesome. Instead the DDS is used for normalisation, similarly to the analysis procedure for the GEMPix data with the CNAO system (section 5.3). The median of the ratios (GEM current / DDS) for each position is plotted against the depth. Taking the median is necessary to reduce the effect of possible outliers mainly due to time misalignment between the ionisation chamber and the DDS. Errors are stated as quartiles, i.e. the error bars cover 50% of the ratios for each position. For the ratio to the FLUKA simulation, the uncertainties are based on the median absolute deviation. Figure 5.42 shows that the current measurement matches well the simulation except for the Bragg peak region. Therefore, the effects in other regions than the Bragg peak are due to the Timepix readout. The ratio of GEM current to FLUKA simulation is used as a correction for further analysis.

5.7.4. Timepix Energy Calibration

The general need and concept for an energy calibration of the Timepix is outlined in section 3.2.7. There are two main difficulties when developing an energy calibration

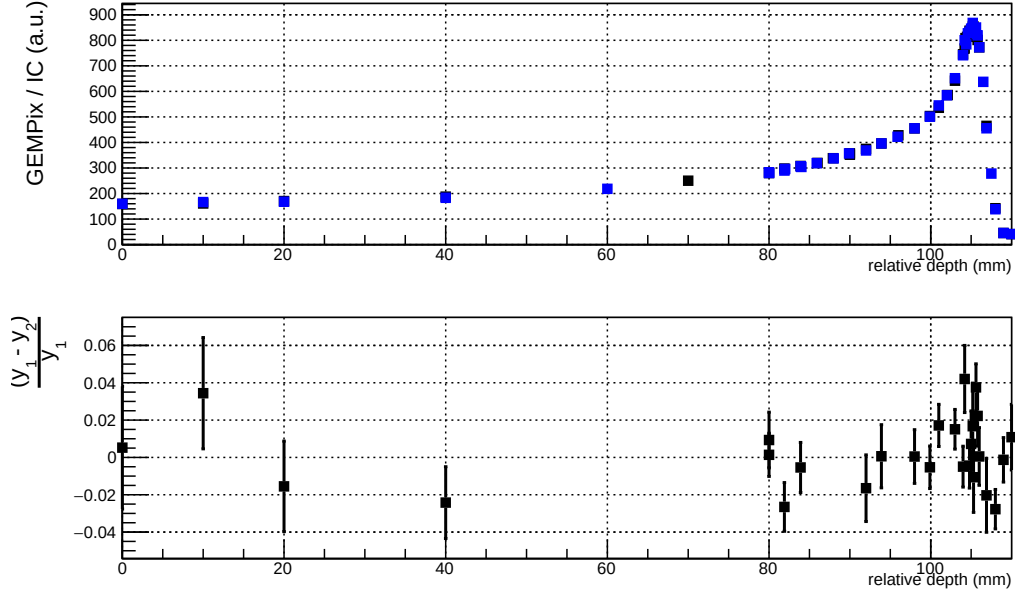


Figure 5.41: Uncorrected Bragg curve data (upper plot) of runs 109/110 and 114/115. The lower plot shows that the relative difference is within $\pm 4\%$, compatible with the statistical fluctuations. For very few depth positions, measurements from only one run are recorded and in this case the ratio cannot be calculated.

for the GEMPix used at CNAO: a calibration for each single pixel is impossible as the charge of single irradiation events (e.g. ^{55}Fe X-rays) is always shared in several pixels and the conditions in beam at CNAO can be hardly reproduced in a laboratory using radioactive sources. In an approach to overcome these issues, a measurement at CNAO is chosen to develop the energy calibration: run 306/307. Figure 5.43 shows the energy deposition expected by the FLUKA simulation plotted against the normalised GEMPix measurement. The surrogate fit function introduced in section 3.2.7 is:

$$y = ax + b - \frac{c}{x - t}. \quad (5.3)$$

GEMPix data y are then corrected by insertion in the inverse of the above function:

$$x = -\frac{b - y - at}{2a} + \sqrt{\left(\frac{b - y - at}{2a}\right)^2 - \frac{(y - b)t - c}{a}} \quad (5.4)$$

where x is the corrected data point.

An important issue is the independence of the data to be corrected from the data to develop this correction function. The best solution found so far, is to choose the run

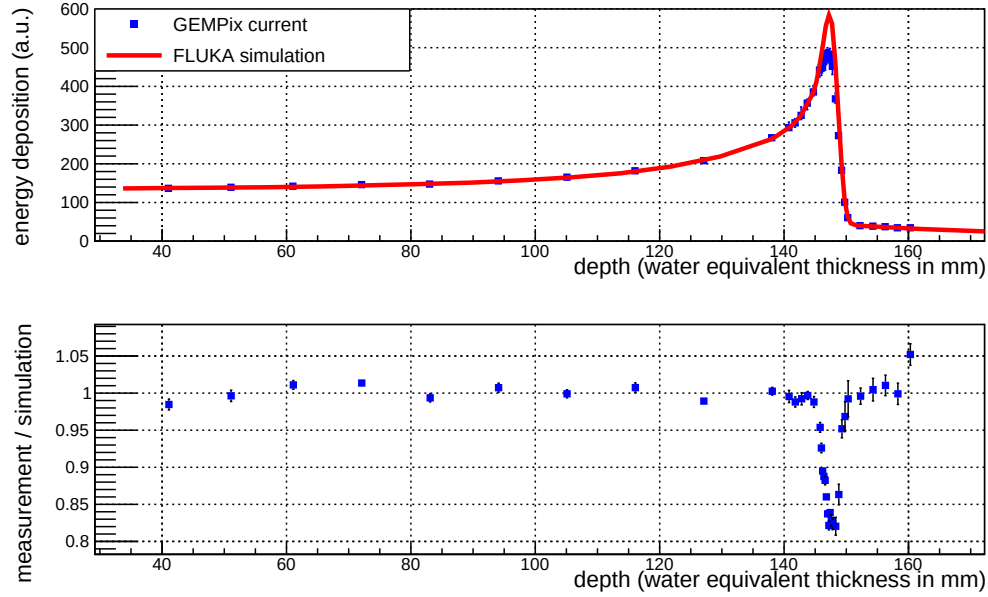


Figure 5.42: Measurements of the current driven by the induction field of run 306/307 compared to the simulation. Error bars in the upper plot are smaller than data points.

306/307 of the shift in April 2018 to develop the correction and apply this correction to the runs of the shift in May 2018. Therefore, a single correction is used for all three carbon ion beam energies. Note that any systematic effect present always in measurements with carbon ions would be corrected for as well by this correction function.

5.7.5. Final Bragg Curve Results

The final results with carbon ions for three different beam energies and corrected as described above by the GEM current measurement and the energy calibration are presented in figure 5.44. Results for different energies are very similar and almost all data points are within $\pm 10\%$ when compared to the simulation (except for a few outliers with larger uncertainties in the tail of the Bragg curve that are contained within $\pm 20\%$). This result presents a major improvement for the project: in the clinical range for carbon ions, stable results with relatively small deviations compared to the simulation over the whole Bragg curve are achieved for the first time. Nevertheless, mismatches are still too large for clinical application.

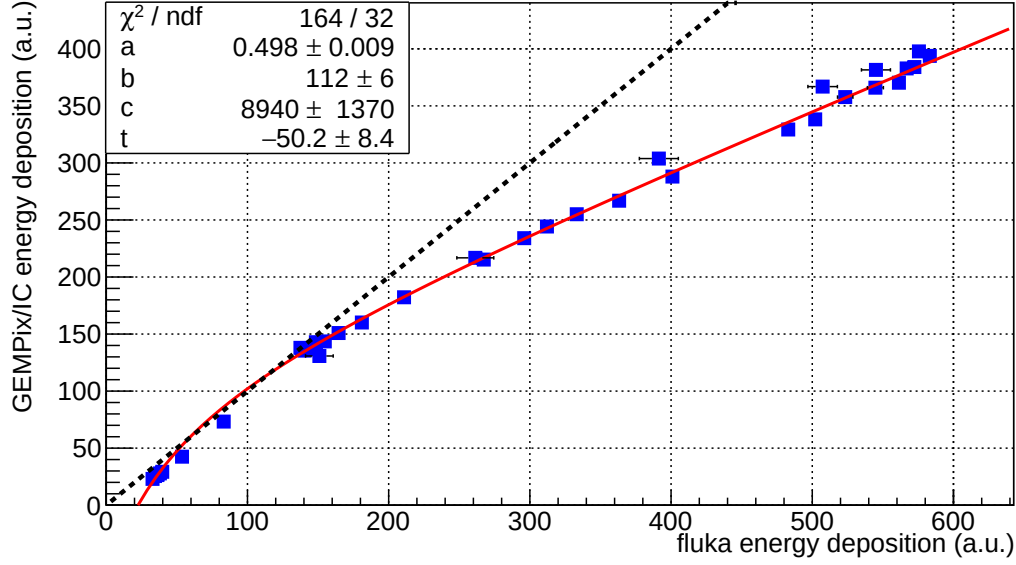


Figure 5.43: Energy calibration of the Timepix readout using run 306/307. For each position the normalised GEMPix measurement is plotted against the FLUKA energy deposition (blue data points). The data do not match the straight line expected for a perfectly calibrated detector (black dashed line). The surrogate function is fit to the data (red solid line).

5.7.6. Investigated Systematic Effects

In the following possible systematic effects are presented. Most of them are ruled out to have a major contribution at the current level of accuracy (i.e. on the level of 10% mismatch).

Pressure, Temperature, Humidity

The temperature, pressure and humidity correction for the GEMPix is presented in section 3.4.5. For measurements at CNAO the described combination of online and offline correction is used. The correction factor is typically a value smaller than 2, as typical operation conditions of the GEMPix are quite far from chosen standard reference values. Therefore, the impact on an absolute value is significant. However changes of this correction factor within a run (which are thus not absorbed by the per-run normalisation factor) are small, typically less than 3%.

Ambient conditions are also important since the ionisation chamber is vented to air. The correction presented in equation 5.1 is applied. The typical value is close to 1 and the variation is completely negligible during a run (less than 1‰).

GEM Saturation

As seen in the GEM current measurements (see figure 5.42), a clear saturation in the Bragg peak is observed in the GEMs. Figure 5.45 shows a dedicated measurement to understand this phenomenon. The saturation increases with the gain as it is expected for electron avalanches approaching the Raether limit (see section 3.1.4). It is possible to push the limit of gain without saturation further by applying an asymmetric gain distribution over the three GEMs as introduced in section 3.1.4. A series of measurements to validate and quantify this improvement at CNAO is not possible but a measurement in the laboratory with an ^{55}Fe source proves the existence of the general effect for the GEMPix (figure 5.46). The linear regime could be extended by more than 50% to higher gains in terms of produced signal.

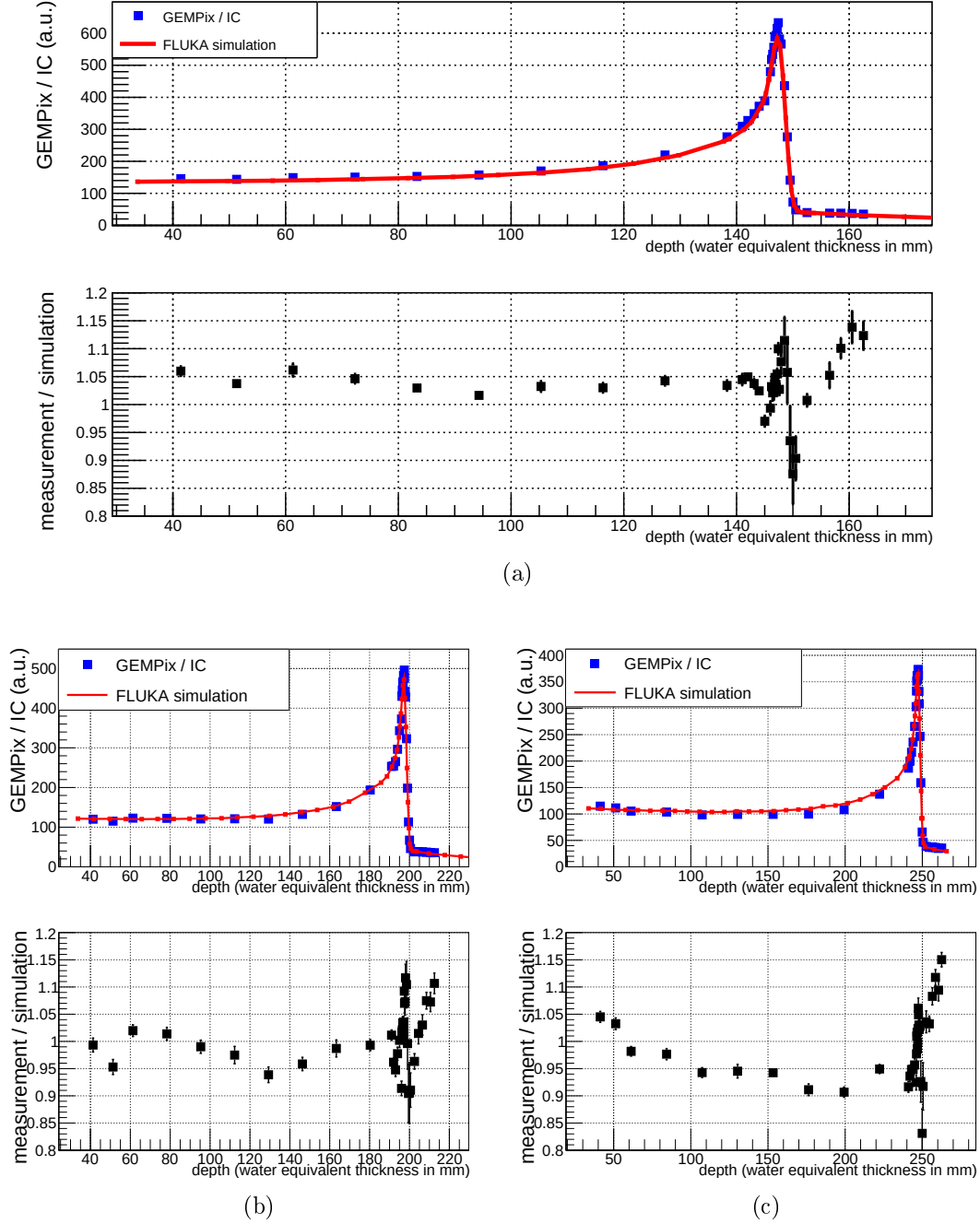


Figure 5.44: Final corrected data for carbon ions with (a) 150 mm (run 403/404), (b) 200 mm (run 413/414) and (c) 250 mm range in water (run 415/416).

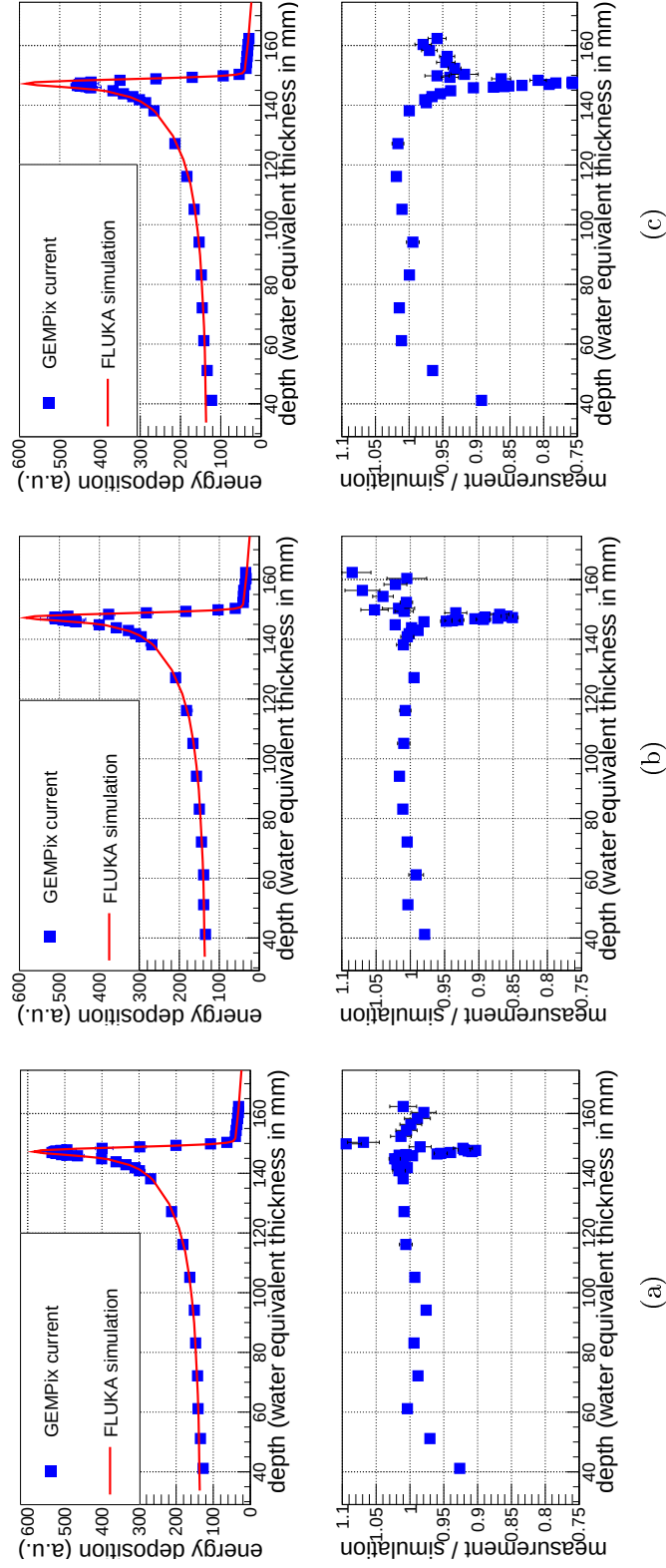


Figure 5.45: Current measurements with different gains: (a) 970 V (run 408/409), (b) 990 V (run 403/404) and (c) 1030 V (run 410/411). The mismatch between measurement and simulation increases with the applied gain (990 V is the gain for the final results presented in section 5.7.5).

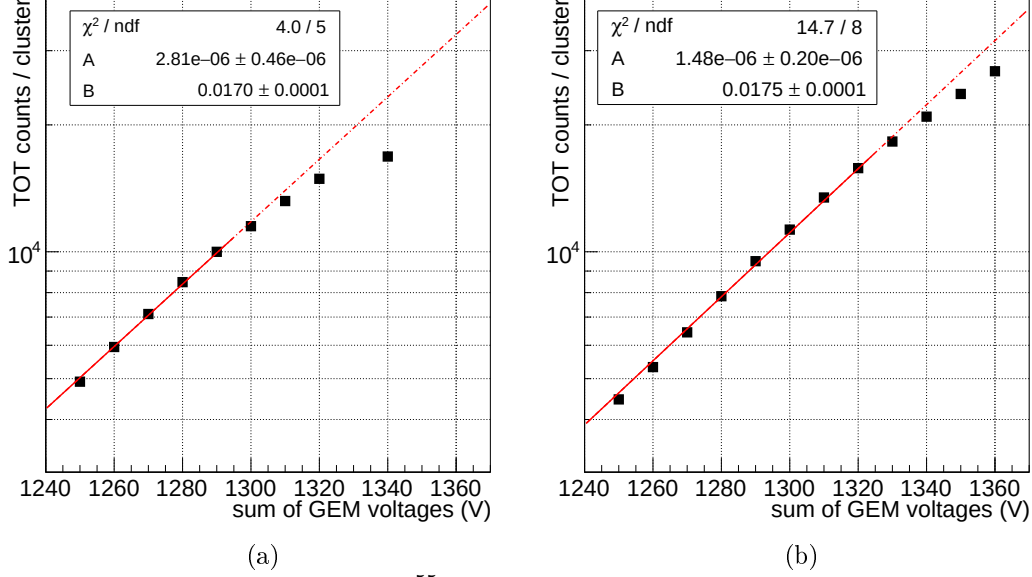


Figure 5.46: Gain scan with an ^{55}Fe source and (a) a balanced gain and (b) a 25% unbalance in the gains. The total gain remains the same but the linear regime for the unbalanced gain is extended to higher total gains.

GEMPix Background

The background in the GEMPix, defined as the signal measured when no spill is present, is subtracted from the measurements during spill. However, the effect of this procedure is typically small, and when the background is subtracted any remaining effect is negligible. However, it is a good check: if the background is large, the GEMPix is most probably not well set up.

Gap Between Readout ASICs

The four Timepix ASICs cannot be mounted without a small gap of approximately 0.2 mm between them⁽¹⁶⁾. To estimate the impact of this effect, the signal of pixels close to the gap is taken into account several times and therefore the missing pixels in the gap are compensated. When taking the signal of the four pixels adjacent to

⁽¹⁶⁾ The size of the gap is measured by taking a picture of all four chips as mounted in the GEMPix and then setting the gap in relation to the known total dimensions of the chips.

the gap twice – i.e. ‘simulating’ the effect of four missing pixels in the gap – the change during a run is typically of the order of 1%.

Alignment of the GEMPix

If the GEMPix is misaligned with respect to the beam axis, the shape of the Bragg curve might be affected depending on the exact situation. Two scenarios are possible: either the GEMPix box inside the water phantom is tilted or the whole water phantom is tilted. In the latter case there is no large effect expected because the amount of water in front of the detector does not change. The change in air has no effect because of the low density. Therefore only the case where the GEMPix box inside the water phantom is tilted is important because this affects the path length of the carbon ions in water. A study showed that a tilt of several degrees⁽¹⁷⁾ would produce an effect of a bit less than 5% in the Bragg peak. However, the tilting of the GEMPix box is measured to be less than 1° and therefore no significant effect is expected⁽¹⁸⁾.

Direct Signal Production in the ASIC

A possible direct signal production as observed during previous measurements at very intense proton beams could lead to a broadened Bragg peak: the signal production in the ASIC would take place on average at some depth and therefore be shifted in depth compared to the energy deposition in the gas volume. This idea could be completely ruled out: the signal contribution when all GEM fields are turned off is measured in beam at CNAO to be around 1%. However, this does not directly translate into a 1% effect on the final Bragg curve because the major effect is the possible change of the superposition of this small, slightly depth-shifted signal and the normal GEMPix signal. Due to the small depth shift, the direct signal contribution is negligible when adding it to the normal GEMPix signal.

Overflow of TOT Pixel Counters

Since the Timepix counters for each pixel are limited to 11,810, an overflow of the counters is possible. The beam intensity, the GEMPix gain, the frame length and the Timepix clock are the main parameters affecting the expected counts per pixel. The

⁽¹⁷⁾In the simplified study a homogeneous beam is assumed. 800 μm difference in depth over the assumed spread out beam size in water of 1 cm would result in a tilt of about 5°.

⁽¹⁸⁾A difference in depth of 2 mm over the GEMPix box size (15 cm) is measured.

pixel counter overflow cannot be corrected well and should be completely avoided. It is checked that the number of pixels with overflow is typically less than 50, which is regarded acceptable out of more than 250,000 pixels and therefore has a negligible effect on the results.

Timepix Threshold Effect

The Timepix threshold is a crucial parameter for the resulting counts per pixel and therefore for the Bragg curve. It is clear from the GEM current measurement (section 5.7.3) that the Timepix signal processing is the main source of mismatch between simulation and GEMPix measurement. If mono-energetic signals are expected (or at least signals with an energy spectrum above a certain minimum energy), the adjustment of the threshold is obvious. However, in the case of a complex radiation field due to secondary particle production – as it is the case in the water phantom – it is very likely that there are particles with very low energies that will be below the threshold. Even for particles with an energy well above threshold, there are always pixels with a small signal because the total charge is shared among many pixels⁽¹⁹⁾. Furthermore, the effect of the threshold, i.e. cutting the part of a signal that is below threshold, is only negligible if the signal is much larger than the threshold. This is not the case for the integrated system. It is difficult to quantify the exact effect of the threshold also because this is an online procedure that cannot be adjusted after the measurements. It is noticed that a more careful adjustment of the GEMPix settings (see section 5.7.7) leads to a better match with the simulation and with the current measurement.

5.7.7. GEMPix Settings Trade-off

The settings of the GEMPix for the final measurements presented in section 5.7.5 are optimised knowing all the systematic effects above and according to the following considerations:

1. The number of electrons arriving to the Timepix pixels should be as high as possible to reduce the threshold effect.
2. Since the GEM current measurement (section 5.7.3) shows saturation, the smallest clinical instantaneous beam intensity is chosen (degrader called F10).

⁽¹⁹⁾In the Bragg peak around 7,500 electrons per primary carbon ion are created. At a typical gain of 100 and a typical sharing of the charge of 100 pixels this results in about 7,500 electrons per pixel. Note that pixels at the edge of a cluster receive less charge than pixels in the centre. The lowest detection threshold of Timepix pixels for noise-free operation is around 700 electrons.

3. The GEM gain has to be chosen quite high (990 V) to have a large number of electrons produced. The resulting saturation in the GEM could be reduced in the future by applying an unbalance in the voltage distribution over the three GEMs. For the results presented here, the GEM currents are measured and the effect is corrected for.
4. The clock of the Timepix should be chosen to be as fast as possible. This increases the resolution for signals just above threshold.
5. A counter overflow of the Timepix pixels has to be avoided. The clock is therefore only set to 4.8 MHz. Another measure to reduce the number of counts to avoid the overflow is to reduce the frame length. However, also this is limited as the absolute dead time between measurements does not strongly depend on the frame length and therefore the relative dead time is almost linearly increased. Furthermore, the integration time of the ionisation chamber cannot be reduced a lot without increasing the noise level. Therefore a frame length of 10 ms is chosen.

5.7.8. 3D Reconstruction

The 3D energy deposition is reconstructed from the same depth scans which are used to measure the Bragg curves (figure 5.44). In a first step the average of the TOT counts for each pixel per position for all measurements with spill is calculated and normalised to the average count per pixel at this position. About 20 pixels per frame with an oddly small or large response are discarded⁽²⁰⁾. Then the counts are weighted with the measured and corrected energy deposition at this depth, i.e. with the values shown in figure 5.44. A linear interpolation between the same pixel at different depths produces a smooth image, which is finally normalised to the maximum dose. Figure 5.47 shows the resulting image.

5.8. Conclusions and Outlook

Several measurements with the GEMPix at CNAO are performed. The goal is to measure the 3D energy deposition of carbon ion and proton beams in water. First, the CNAO water phantom is used and a proof-of-concept is finalised, showing the

⁽²⁰⁾For example the counts of pixels with a response more than five times that of the neighbouring pixel are not taken into account but the counts of the neighbouring pixel is accounted for twice. Note that the number of affected pixels (typically around 20) is small compared to the total number of pixels (262,144).

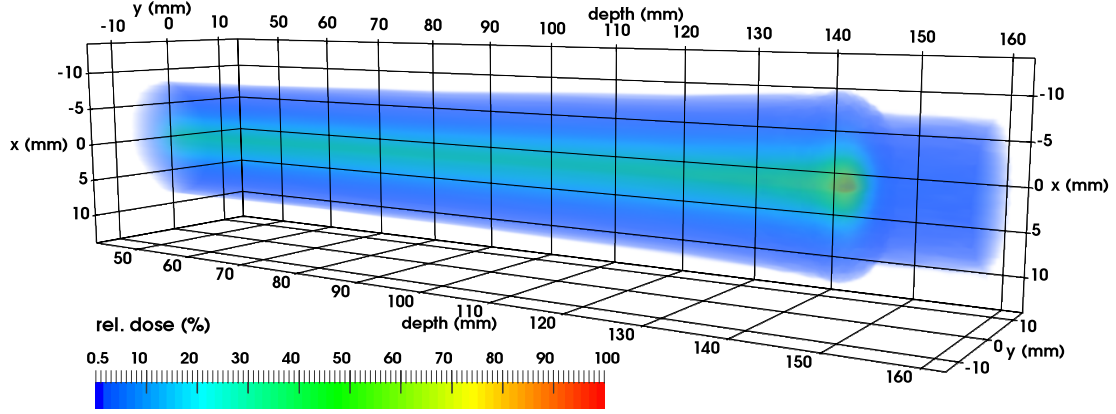


Figure 5.47: The 3D energy reconstruction of run 403/404 (carbon ions with 150 mm range). The beam enters the water on the left and spreads out. The tail behind the Bragg peak (on the right side in the image) is well visible but the exact shape depends strongly on the chosen minimum dose which is in this case 0.5% of the maximum dose.

general possibility to use the GEMPix for this purpose but also showing technical limitations of the set-up. Several of these limitations are overcome by developing the integrated system which requires a lot of effort before measurements at CNAO are performed: the hardware needs to be completed and set up, control and analysis software to be written and test measurements to be performed. Finally, a stand-alone system is achieved that does not require information such as a trigger from the accelerator and that can be set up relatively fast in a treatment room. The high quality of the data for carbon ions acquired with the integrated system allows an in-depth understanding of the measurements. Issues such as the energy calibration of the readout and the GEM current measurements are discovered and solutions proposed. The final data set, after calibrations, matches the FLUKA simulation for different beam energies for most data points within $\pm 10\%$. This represents a major improvement. Several other sources of systematic errors are investigated and need to be under control before mismatches of around 1% could be achieved in the future. The measurements with protons are not of the same quality yet and better GEMPix settings are necessary before an in-depth analysis similar to the one for carbon ions can be performed.

However, several requirements for a detector to be used for quality assurance of clinical proton and carbon ion beams or patient treatment plan verification cannot be met with the current detector set-up. An overview of requirements and the current status is provided below. An ideal detector has to be designed to:

- Perform measurements with all clinical beam settings, e.g. carbon ions with maximum $2 \cdot 10^8$ particles per second and protons with maximum $1 \cdot 10^{10}$ particles per second at a hadron therapy facility like CNAO. Currently, measurements at CNAO are mainly performed with carbon ions at the smallest clinical beam intensity of $2 \cdot 10^6$ particles per second. The majority of proton therapy centres are cyclotron facilities and beam settings at these facilities are different compared to synchrotron-based facilities. Therefore measurements at such a facility would be of interest.
- Be radiation hard. Radiation hardness of the Timepix and so-called ageing of GEMs have been investigated (see sections 3.1.5 and 3.2.8) but need to be checked for a possible future detector set-up with the typical irradiation conditions in a clinical facility.
- Have a sensitive area of $20 \times 20 \text{ cm}^2$ as this is typically the maximum size of the treatment field. This is much larger than the current readout area of $3 \times 3 \text{ cm}^2$.
- Have a readout with a spatial resolution better than approximately 0.5 mm. The Timepix chip has a $55 \mu\text{m}$ pixel pitch which may be even too small because the spatial resolution is better than needed and the charge per pixel is small (see below).
- Avoid any significant dead time because it should not miss any of the delivered dose of a treatment plan. Currently the dead time is more than 90%.
- Have a small footprint and use a gas that can be handled in a clinical facility. While conventional ionisation chambers are vented to air, the GEMPix is usually used with a dedicated detection gas such as $\text{Ar}:\text{CO}_2:\text{CF}_4$ (45:15:40).
- Allow a fast measurement procedure since the time needed per measurement is an important cost factor. This includes a fast set-up, a fast data acquisition and an online data analysis. The integrated system which is currently tested allows a quick set-up and an online data analysis was developed. However, the dead time limits the acquisition speed.
- Handle the fact that the charge per pixel is rather low. In the current set-up, approximately 7,500 electrons per primary carbon ion are produced in the detector at the Bragg peak. At the usual gain of 100 this results in 750,000 electrons distributed over typically 100 pixels. The gain most likely needs to be further reduced in order to avoid saturation in the GEMs and reduce the discharge probability.

- Be independent of ambient conditions such as pressure and temperature. A temperature and pressure correction for the GEMPix has been developed but may need improvements and modifications for a new detector set-up.

First ideas to overcome the above mentioned issues are currently under investigation. The latest version of the Timepix ASIC, the recently developed Timepix 2, could overcome some problems. However, the issue of larger readout areas remains the same as of the Timepix. Since the signal created in the GEMs matches well the simulation except for saturation in the Bragg peak and since GEMs can be easily produced with a larger area, other readout options than the Timepix are tested. The optical photons produced in Ar:CO₂:CF₄ (45:15:40) can also be used to measure the Bragg curve (see for example [70]).

Another application of the GEMPix related to radiation therapy but not investigated in detail so far is microdosimetry. Microdosimetry is the ‘systematic study and quantification of the spatial and temporal distribution of absorbed energy in irradiated matter’ [168, p. 1]. While the absorbed dose is the standard reference quantity in radiation physics and radiation protection, it is a macroscopic quantity insufficient to understand the effects of ionising radiation at the cellular level and to explain the RBE of different types of radiation. For example, damage to the deoxyribonucleic acid (DNA) of a cell and therefore the possible cell death does not only depend on the absorbed dose but also requires knowledge of microdosimetric quantities. This knowledge is crucial for improvements in radiation therapy. With the standard detector for microdosimetry – the tissue equivalent proportional counter (TEPC) – no spatial information in the detection volume is obtained and the magnification is not large enough to study radiation effects in detail at the size of the human cell structure. The GEMPix would significantly improve the spatial resolution allowing to go down to the 100 nm level due to the small pixel size and the magnification achieved in tissue equivalent gas compared to tissue. Therefore it would pave the way to new research fields, which will add to the knowledge of irradiation processes and may help to improve radiation therapy.

6. Conclusions and Outlook

The aim of this thesis is to exploit the capabilities of the GEMPix detector for two applications, namely the measurements of ^{55}Fe content in activated samples of radioactive waste and the energy deposition measurements in water for hadron therapy. Before the two applications are investigated, the GEMPix is improved regarding the correction of temperature, pressure and humidity changes in the detection gas. Characterisation measurements such as gain scans and the spatial uniformity of the gain over the sensitive area are reported. A stable response is achieved over more than one week when avoiding the investigated effects due to the switch-on of the detector and when applying the developed online HV correction.

Forty-five samples from radioactive waste at CERN are used to calibrate the GEMPix response to specific activity. Measurements of the ^{55}Fe content require a dedicated procedure consisting of calibration, background and sample measurements. In total, the measurements per sample take around 4.5 hours. As a proof-of-concept, the GEMPix results for the same 45 samples are compared to the results obtained by the conventional method, the radiochemical analysis. The detection limit of the GEMPix based on the background counts is calculated as well as the sensitivity to the Swiss clearance limit of 30 Bq/g at the time the analysis was performed. The GEMPix is potentially sensitive to this clearance limit but a complete uncertainty study is needed. This is likely to increase the uncertainties assigned to the GEMPix measurements. However, since the Swiss clearance limit was increased by more than a factor of 30 to 1 kBq/g in 2018, the GEMPix is believed to be well sensitive to the new clearance limit.

In hadron therapy, one of the main cancer treatment modalities, quality assurance is an important issue requiring well suited detectors to measure the energy deposited by the hadron beam in water. Typically each patient treatment plan is verified by delivering the planned dose into a water phantom and comparing results measured with an array of ionisation chambers and predicted by the treatment planning system. The Timepix readout of the GEMPix has pixels with an area of $55 \times 55 \mu\text{m}^2$ each and therefore a spatial resolution superior to that of an array of ionisation chambers. The GEMPix is first mounted on the CNAO water phantom but several issues are discovered leading to the development of the integrated system. It consists of a commercial water phantom with a motorised positioning system, an ionisation

chamber for reference measurements and the GEMPix. The developed data acquisition software enables automatic scans of set depth positions to measure the Bragg curve. Data are analysed preliminarily online. The data quality compared to the first setup is significantly improved and the smooth Bragg curves with approximately 1% statistical fluctuations allow for in-depth studies of systematic effects. Several effects are investigated and most of them do not affect the results significantly. The set-up is simulated in FLUKA, carefully testing set-ups with simplified geometries before. An energy calibration similar to the common Timepix calibration is applied and the discovered saturation of the GEM signal is corrected for. The final results match the simulation within $\pm 10\%$ for most data points for three different clinical carbon ion beam energies. This represents a major improvement but is still insufficient for clinical application. For measurements with a proton beam this data quality has not yet been achieved. The 3D energy deposition is reconstructed from the same depth scans.

A larger area than the current $2.8 \times 2.8 \text{ cm}^2$ is required for quality assurance in radiation therapy since the typical maximum radiation field is $20 \times 20 \text{ cm}^2$ large. The GEMs are available in the required size but it is improbable to achieve such an area with Timepix ASICs. Therefore, other readouts need to be investigated. Tests at cyclotron based proton therapy centres will be of interest since beam characteristics are different compared to synchrotrons (e.g. at CNAO) and since the majority of proton therapy centres use a cyclotron. A possible future application of the GEMPix related to radiation therapy is microdosimetry, i.e. the study of the spatial and temporal distribution of the absorbed dose. Microdosimetric measurements are needed to understand the irradiation effects in detail and to improve radiation therapy. The GEMPix could potentially increase the spatial resolution and add spatial information in the investigated gas volume.

A. Appendix

A.1. Timepix Technical Specifications

Table A.1 provides the technical specifications of the Timepix ASIC and figure A.1 shows the schematic readout of a Timepix pixel.

Table A.1.: Technical specifications of the Timepix [169].

General	
Parameter	Value
CMOS technology	0.25 μm
Pixel matrix	256 x 256
Design	CERN
Features	• Single energy threshold (adjustable per pixel with 4 bits) • Three modes of operation: (1) single particle counting (2) Time over Threshold (TOT) and (3) Time of Arrival (TOA) • Can be combined with Gas Gain Grid to readout electron deposition in a gas detector • Hit rate 100 kHz • 3-side buttable
Power Supply	Two independent 2.2 V power supplies for the analogue and digital part
Number of transistors	$\approx$ 36 million

Table A.1.: Technical specifications of the Timepix [169] (continued).

Analogue front end (pixel cell)	
Parameter	Value
Baseline shift preamplifier output	112 e ⁻ rms
Signal polarity	Positive and negative
Detector capacitance	
Leakage current	-10 to 20 nA
TOT monotonicity	Up to 200 ke ⁻
Time to peak	110 ns
Noise	75 e ⁻
Analogue static power consumption	6 μ W
Analogue power consumption	440 mW
Digital part (pixel cell + periphery)	
1 counter/shift register	14 bits (11810 counts)
periphery	• 13 8-bit DACs to set voltages in the chip • 1 256-bit Fast Shift Register to write in o read out the sensitive area • 127 I/O pads • LVDS drivers and receivers (configuration of the chip in serial mode) • Parallel 32.bit CMOS bus (chip readout can be serial or parallel)
Readout time in serial mode (100 MHz clock)	9 ms (102 Mbps)

A.2. Gain Scan with ²⁴¹Am

A gain scan similar to the one described in section 3.4.1 is performed with an ²⁴¹Am source. Figure A.2 shows the number of clusters against the sum of the GEM voltages. In order to check the linearity of the TOT response (figure A.3), the most probable TOT value close to the maximum of the distribution is determined⁽¹⁾. The obtained results are similar to the one of ⁵⁵Fe, except for a shift to lower voltages because the α -particles are more ionising than the 5.9 keV photons of ⁵⁵Fe.

⁽¹⁾The spectrum is observed to have a similar shape over the applied different gains with a most probable value relatively close to the maximum.

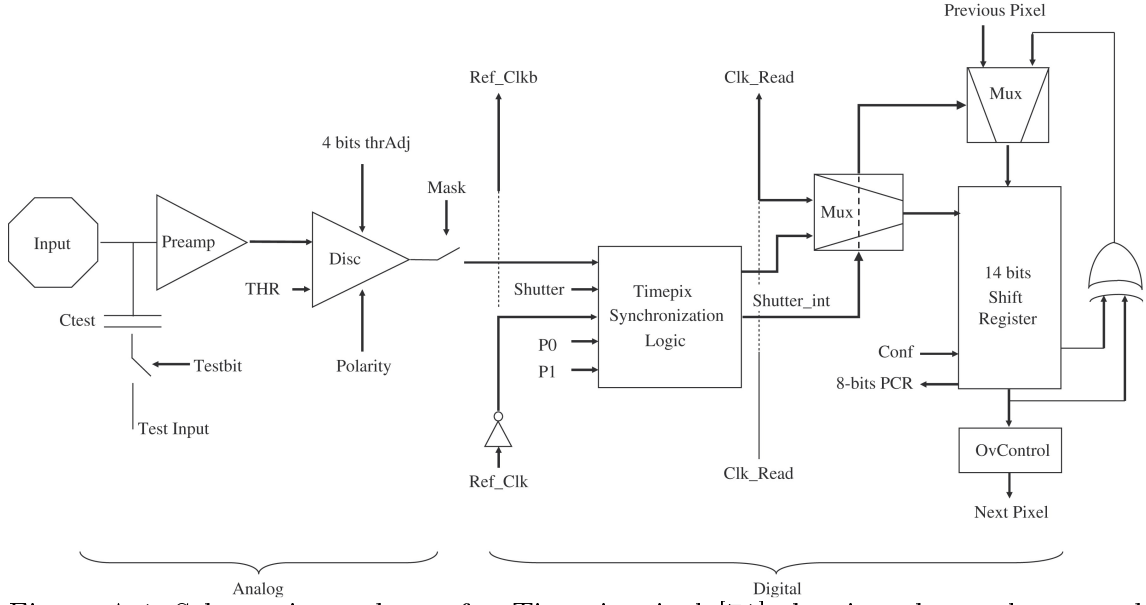


Figure A.1: Schematic readout of a Timepix pixel [71] showing the analogue and digital part.

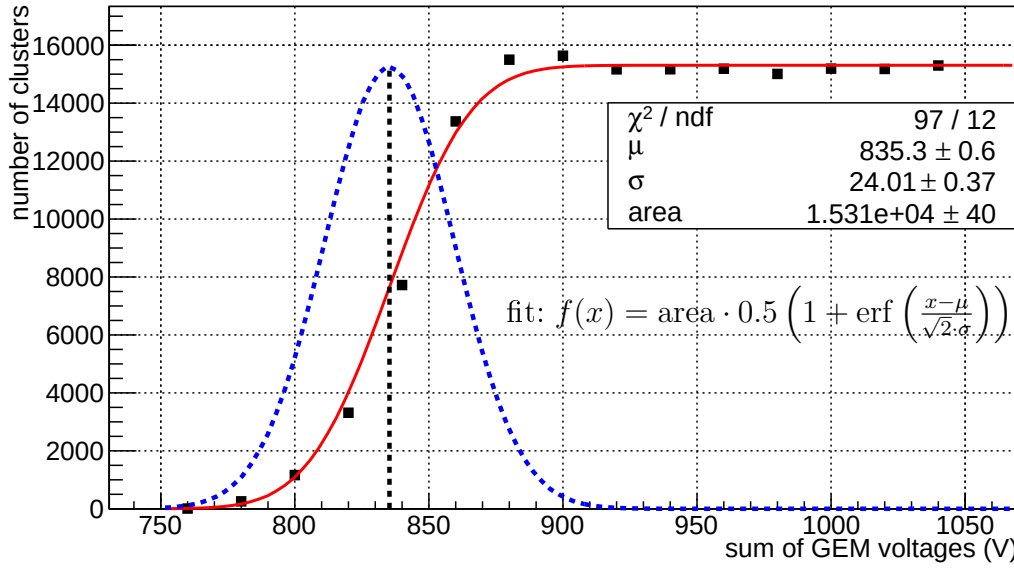


Figure A.2: Gain scan with an ^{241}Am source: the number of clusters against the total gain voltage (black) are fit by an integrated Gaussian function (red solid line). The derivative of the fit function (i.e. a Gaussian function, blue dashed line) is drawn for comparison, with the vertical black dashed line showing the mean value at which 50% of the events are detected.

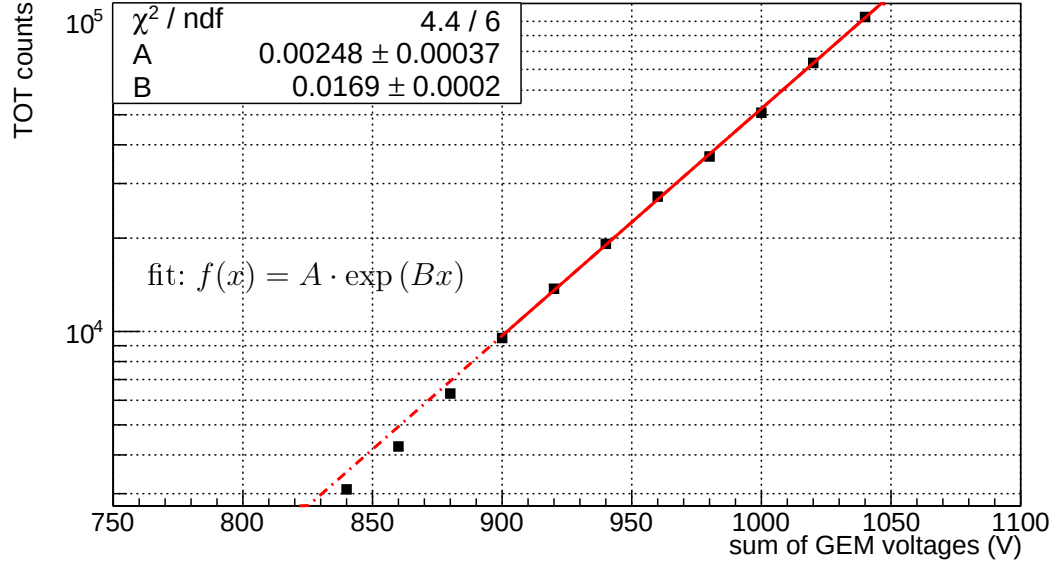


Figure A.3: Gain scan with an ^{241}Am source: the most probable TOT values for each gain against the total gain voltage (black) are fit well by an exponential function (red) above 900 V.

A.3. Gain Scan with Light

A gain scan similar to the one described in section 3.4.1 is performed using the room light. Most probably, the signal measured stems from the UV component of the light, as the sensitivity of the GEMPix to UV light is demonstrated in section 3.4.6. Figure A.4 shows the number of clusters against the sum of the GEM voltages. Since the plateau is just reached at the highest voltage and yet higher voltages are not applied to avoid discharges, the linearity check and resolution measurement performed for ^{55}Fe are not possible here. The shift to higher voltages compared to the measurements with ^{55}Fe is due to the smaller energy deposition of the UV photons.

A.4. Parameters Saved by Cluster Analysis

Table A.2 provides an overview and explanation of all parameters saved when the online cluster analysis is used.

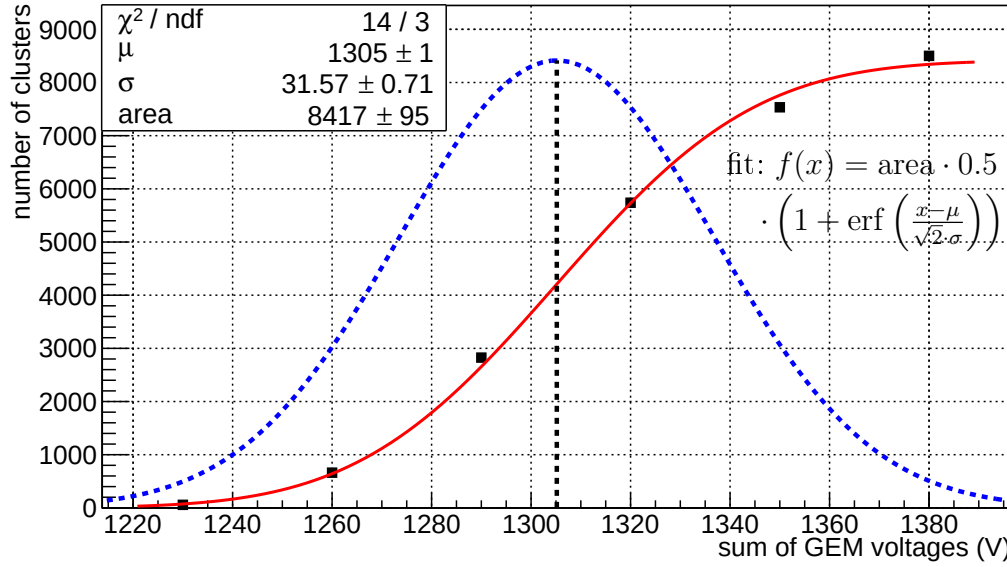


Figure A.4: Gain scan with the room light: the number of clusters against the total gain voltage (black) are fit by an integrated Gaussian function (red solid line). The derivative of the fit function (i.e. a Gaussian function, blue dashed line) is drawn for comparison, with the vertical black dashed line showing the mean value at which 50% of the events are detected.

Table A.2.: Parameters saved when the online cluster analysis is used.

Name	Explanation
time	time stamp in ms
event	event number
numclu	number of clusters in this event
clunum	cluster number
type	cluster type : 1=dot, 2=small blob, 3= curly track, 4=heavy blob, 5=heavy track
size	cluster size
innpix	number of internal pixels
borpix	number of pixels of the cluster border
sizex	dimension of the cluster in X direction
sizey	dimension of the cluster in Y direction
volume	total TOT counts (energy released by the cluster)
maxdist	maximum distances between two pixels inside the cluster
flatx	x position of the cluster
flaty	y position of the cluster

Table A.2.: Parameters saved when the online cluster analysis is used (continued).

Name	Explanation
centx	x position of the cluster weighted by the charge
centy	y position of the cluster weighted by the charge
inline	pixels on straight line
covex	convex hull of the cluster
region	parameter to define subregions on the detector

A.5. ^{55}Fe Results

Table A.3 provides additional information regarding the measurements of the ^{55}Fe content: the third and the fourth column show the GEMPix raw and background counts in 7200 s respectively. A background count number in brackets means that the background is not measured, as explained in section 4.3. The last column provides the net counts normalised to 1000 s.

Table A.3.: Results of all samples measured to determine the ^{55}Fe content.

no.	TREC /ID	GEMPix raw counts in 7200 s	GEMPix background counts in 7200 s	GEMPix net counts per 1000 s
1	CR-028446	43 ± 6.6	$(50) \pm 7$	-0.97 ± 1.34
2	CR-028418	33 ± 5.7	$(50) \pm 7$	-2.36 ± 1.27
3	CR-028557	40 ± 6.3	$(50) \pm 7$	-1.39 ± 1.32
4	CR-037144	29 ± 5.4	$(50) \pm 7$	-2.92 ± 1.23
5	CR-037138	42 ± 6.5	$(50) \pm 7$	-1.11 ± 1.33
6	CR-028426	46 ± 6.8	$(50) \pm 7$	-0.56 ± 1.36
7	CR-037654	66 ± 3.1	54 ± 3	1.67 ± 0.57
8	CR-028406	48 ± 6.9	$(50) \pm 7$	-0.28 ± 1.37
9	CR-037147	51 ± 7.1	$(50) \pm 7$	0.14 ± 1.40
10	CR-028553	47 ± 6.9	$(50) \pm 7$	-0.42 ± 1.37
11	CR-036728	41 ± 6.4	$(50) \pm 7$	-1.25 ± 1.32
12	CR-028432	52 ± 7.2	$(50) \pm 7$	0.28 ± 1.40
13	CR-037148	55 ± 7.4	$(50) \pm 7$	0.69 ± 1.42
14	CR-028384	58 ± 7.6	$(50) \pm 7$	1.11 ± 1.44
15	CR-037140	63 ± 7.9	$(50) \pm 7$	1.81 ± 1.48
16	CR-028382	58 ± 7.6	$(50) \pm 7$	1.11 ± 1.44
17	CR-028430	65 ± 8.1	$(50) \pm 7$	2.08 ± 1.49
18	CR-028354	71 ± 8.4	$(50) \pm 7$	2.92 ± 1.53

Table A.3.: Results of all samples measured to determine the ^{55}Fe content (continued).

no.	TREC /ID	GEMPix raw counts in 7200 s	GEMPix background counts in 7200 s	GEMPix net counts per 1000 s
19	CR-028448	68 ± 8.2	$(50) \pm 7$	2.50 ± 1.51
20	CR-037146	84 ± 9.2	$(50) \pm 7$	4.72 ± 1.61
21	CR-028400	95 ± 9.7	$(50) \pm 7$	6.25 ± 1.67
22	CR-028428	71 ± 8.4	$(50) \pm 7$	2.92 ± 1.53
23	CR-028394	67 ± 8.2	$(50) \pm 7$	2.36 ± 1.50
24	CR-036727	73 ± 8.5	$(50) \pm 7$	3.19 ± 1.54
25	CR-028555	73 ± 8.5	$(50) \pm 7$	3.19 ± 1.54
26	CR-036725	79 ± 8.9	$(50) \pm 7$	4.03 ± 1.58
27	CR-028388	82 ± 9.1	$(50) \pm 7$	4.44 ± 1.60
28	CR-028422	128 ± 11	$(50) \pm 7$	10.8 ± 1.9
29	CR-028392	132 ± 12	$(50) \pm 7$	11.4 ± 1.9
30	CR-028390	453 ± 21	289 ± 17	22.8 ± 3.9
31	CR-028412	232 ± 17	$(50) \pm 7$	25.3 ± 2.6
32	CR-028444	214 ± 16	42 ± 7	24.0 ± 2.4
33	CR-028434	235 ± 15	46 ± 7	26.3 ± 2.3
34	CR-028386	315 ± 18	52 ± 7	36.5 ± 2.7
35	CR-028374	571 ± 24	139 ± 12	60.0 ± 3.7
36	CR-028408	463 ± 22	60 ± 8	56.0 ± 3.2
37	CR-037656	1101 ± 33	44 ± 7	147 ± 5
38	CR-037450	582 ± 24	76 ± 9	70.3 ± 3.6
39	CR-037653	552 ± 24	50 ± 7	69.7 ± 3.4
40	CR-028424	630 ± 25	66 ± 8	78.3 ± 3.7
41	CR-028410	508 ± 23	$(50) \pm 7$	63.6 ± 3.3
42	CR-028376	1047 ± 32	187 ± 14	119 ± 5
43	CR-028414	1159 ± 38	187 ± 15	135 ± 6
44	CR-037657	1928 ± 44	88 ± 9	256 ± 6
45	CR-037655	5135 ± 72	196 ± 14	686 ± 10

A.6. Technical Specifications of PTW 34080 Ionisation Chamber

Table A.4 provides the technical specifications of the PTW 34080 ionisation chamber.

Table A.4.: Technical specifications of the PTW 34080 Ionisation Chamber [170].

Device designation	Bragg Peak Chamber Type 34080
Manufacturer	PTW-Freiburg
Particular design characteristics	• plane-parallel chamber • vented to air • waterproof • guard ring • perturbation free
Measuring quantities	relative measurements
Reference quality	^{60}Co
Nominal sensitive volume	10.5 cm^2
Effective point of measurement (reference point)	inside of entrance window, centre
Reference direction of incidence	perpendicular to the entrance window
Nominal response	325 nC/Gy (reference field $^{60}\text{Co D}_W$)
Chamber voltage	nominal: $+400\text{ V}$ maximal: $\pm 500\text{ V}$
Leakage current	$\leq \pm 100\text{ fA}$
Cable leakage	$\leq 1\text{ pC}/(\text{Gy cm})$
Cable length	min. bending radius 20 mm (static) min. bending radius 50 mm (for up to 50 repetitions)
Maximum dose rate during continuous radiation (at nominal voltage of 400 V)	99.0% saturation: 42 Gy/s 99.5% saturation: 21 Gy/s
Maximum dose per radiation pulse (at nominal voltage of 400 V)	99.0% saturation: 1.8 mGy 99.5% saturation: 0.9 mGy
Ion collection time (at nominal voltage of 400 V)	$67\text{ }\mu\text{s}$
Polarity effect	$\leq \pm 1\%$

Table A.4.: Technical specifications of the PTW 34080 Ionisation Chamber [170] (continued).

Directional response	$\leq \pm 1\%$ for tilting around the detector axis up to $\pm 5^\circ$ $\leq \pm 1\%$ for tilting perpendicular to the detector axis up to $\pm 5^\circ$
Transient periods for temperature equilibrium pressure equilibrium	4 min/K to 5 min/K <15 s
Pre-irradiation	not required
Stabilisation time	The response after 15 minutes and 2 hours differs by less than $\pm 0.5\%$ from the value after 1 hour.
Post irradiation leakage	signal drops to <1% within 10 s after irradiation
Entrance window	0.1 mm lacquer, 0.5 mm PMMA, 0.02 mm graphite
Area density	72 mg/cm ²
Water-equivalence	0.7 mm for photons
Electrode material	PMMA, graphite-coated

A.7. Technical Specifications of PTC IC101 Ionisation Chamber Readout

Table A.5 provides the technical specifications of the PTC IC101 ionisation chamber readout.

Table A.5.: Technical specifications of the PTC IC101 Ionisation Chamber Readout [171].

Operating principle	Gated integrator (charge integrating amplifier).
Integration capacitor	Dual, software selectable. Default values 100 pF and 3300 pF.
Input noise	<200 fA rms unloaded (1 s integration, 10 pF capacitor at $\leq 25^\circ\text{C}$ ambient).
Input offset	<10 pA, 15°C to 25°C , <3 pA typical. Offset can be removed by zero subtraction.
Input impedance	<3 k Ω
Input protection	Back to back fast diodes, spark gap.
Stability	Output drift <200 fA/hour at $(25 \pm 1)^\circ\text{C}$ ambient after stabilisation.

Table A.5.: Technical specifications of the PTC IC101 Ionisation Chamber Read-out [171] (continued).

External accuracy	Better than 0.5% of full scale in use, integration time 500 μ s to 1 s, after calibration with built-in current source.
Pre-defined current ranges	1 nA, 8 nA, 10 nA, 100 nA, 1 μ A, 10 μ A, 100 μ A, 200 μ A
Integration time	User selectable, 100 μ s to 10 s.
External gate input	TTL 10 k Ω impedance
Trigger modes	Internal (autorun), external_start, external_start_stop, external_start_hold.
Digitisation	16 bit bipolar over ± 10 V integrator output range.
Averaging modes	Multiple conversions per integration; multiple integrations per reading to increase digital resolution up to 20 bits.
Auxiliary HV PSU	(Factory option) 0 to 3000V programmable (polarity and maximum voltage factory selectable), 1 W max at full voltage and current.
Noise and ripple	<0.01%
Power input	(24 $\pm$ 2) V DC, 300 mA typ, 500 mA max.
Controls	Two rotary switches for loop address and comms mode/ baud rate.
Displays	Six status LEDs (power, comms mode, device status). ‘HV on’ LED.
Case material	Stainless steel sheet.
Weight	0.7 kg (1.5 lb)
Operating environment	10 $^{\circ}$ C to 35 $^{\circ}$ C (15 $^{\circ}$ C to 25 $^{\circ}$ C recommended to reduce drift and offset), <70% humidity, non-condensing, vibration <0.1 g all axes (1 Hz to 100 Hz). Vibration must be as low as possible to measure at the lower limit of the dynamic range.
Shipping and storage environment	–10 $^{\circ}$ C to 50 $^{\circ}$ C, <80% humidity, non-condensing, vibration <2 g all axes, 1 Hz to 100 Hz.

A.8. Measurements with PTW 34080 Ionisation Chamber at the Calibration Laboratory Using a ^{137}Cs source

Measurements with a ^{137}Cs source are performed in the Calibration Laboratory. For this, the 3 TBq ^{137}Cs source, which is located in the large measurement hall,

is used. Figure A.5 shows a picture of the PTW ionisation chamber in the large hall at the Calibration Laboratory. The chamber is supplied and read out in the same way as for the measurements with the ^{60}Co source presented in section 5.5.1. Five measurements are performed. Only the distance between source and chamber is changed between 82 cm to 120 cm. The measured currents are low due to the lower activity of the source compared to the ^{60}Co source. Therefore the offset is measured and subtracted from each measurement. An estimated uncertainty of 1% is applied to the current measurements. Figure A.6 shows that the measured current follows well the expected $1/d^2$ -relation. Figure A.7 shows the linearity. The response of the ion chamber is well linear but yields a different value compared to the nominal response, as the nominal response is measured with a ^{60}Co source.

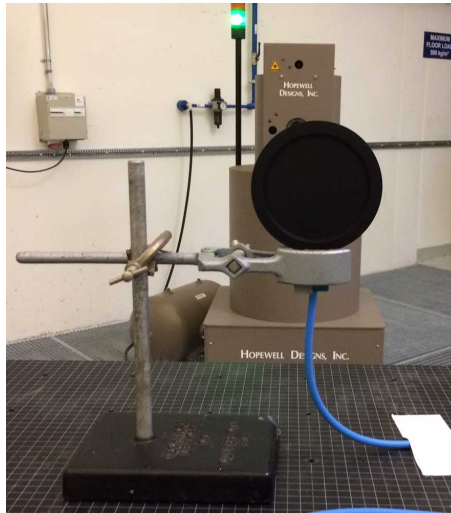


Figure A.5: The ionisation chamber (foreground) in front of the source system containing the ^{137}Cs source in the large hall of the Calibration Laboratory.

A.9. Additional Material for Measurements at CNAO with the PTW 34080 Ionisation Chamber

Figure A.8 shows ratio of the two DDS detectors for run 1 and figure A.9 shows the mean value and the sigma of the Gaussian fits to the ratio of the two DDS detectors for all runs. From these values, the mean correction factor between the two DDS detectors for our sets of runs is calculated to be 6.5%. The sigma of the distribution is 0.41%. An uncertainty of 0.3% is applied on the DDS counts – assuming that

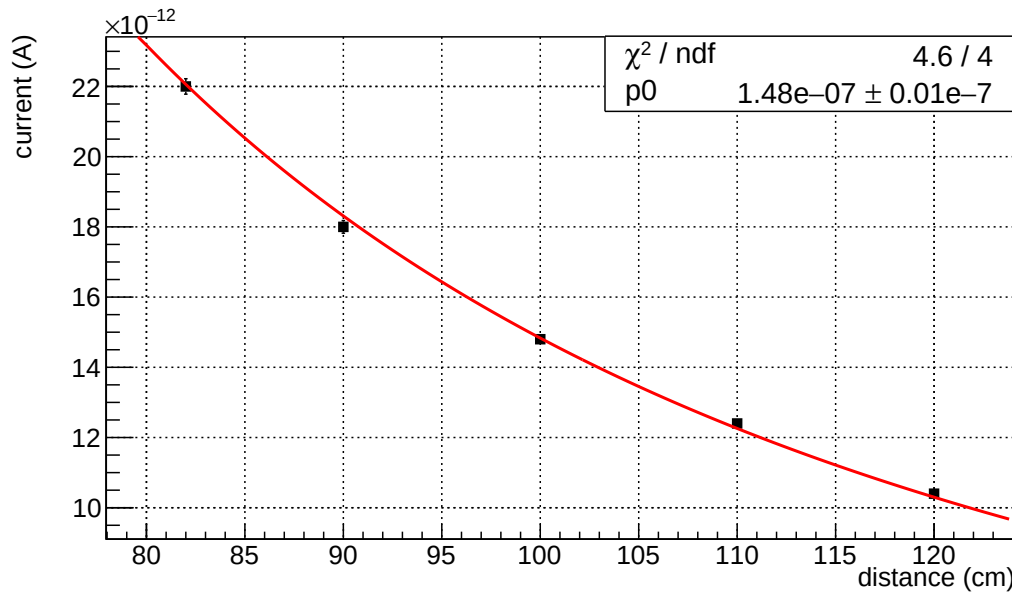


Figure A.6: The measured current follows well the expected $1/\text{distance}^2$ -relation (fit function: $f(x) = p_0/d^2$).

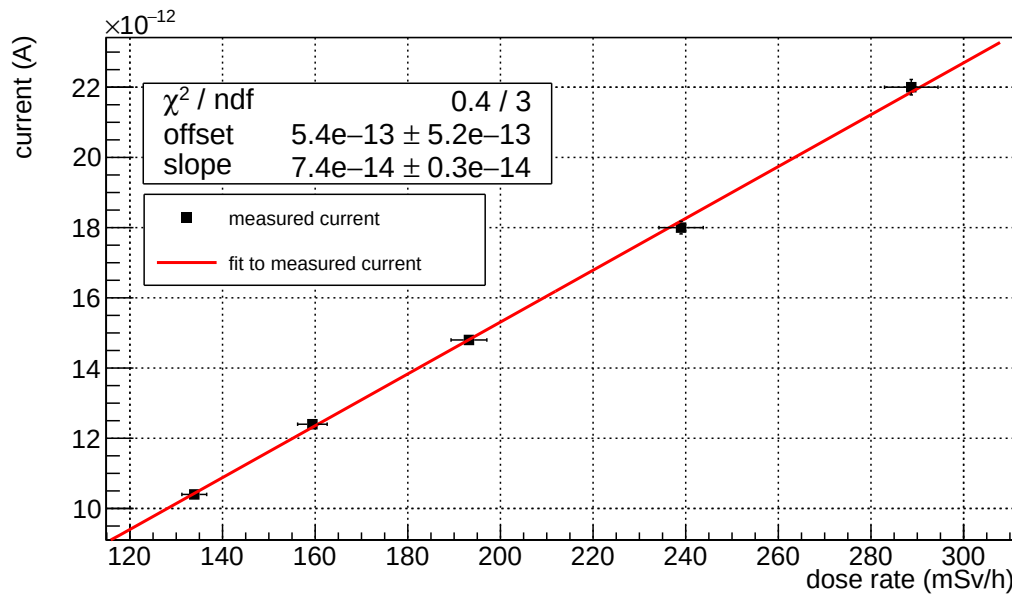


Figure A.7: The measured response is well linear, yielding (27 ± 2) nC/Gy.

both DDS uncertainties are of the same size and independent and therefore would add up quadratically to 0.41%.

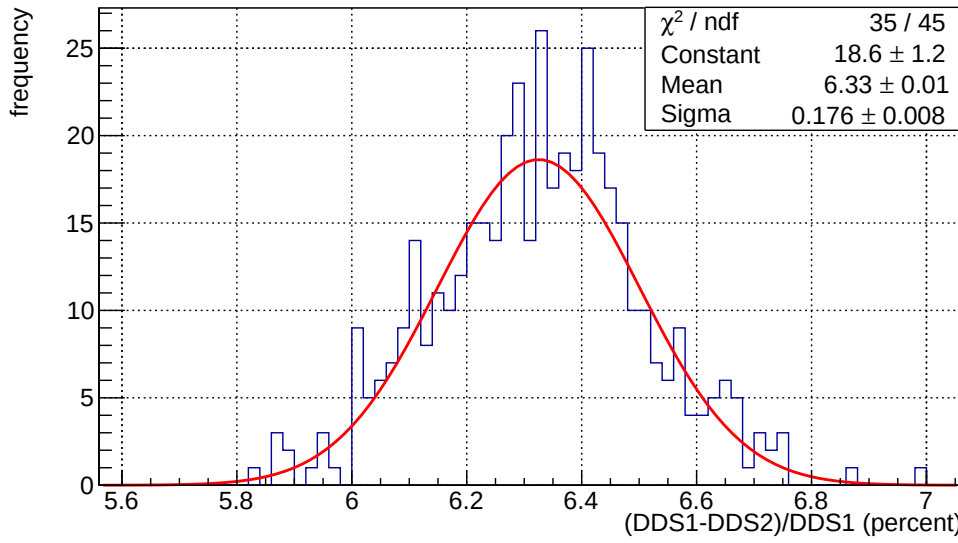


Figure A.8: Ratio of the two DDS detectors for run 1. A correction factor is applied between the two DDS detectors. The size of the fluctuations of this correction factor for a single run is given by the sigma of the fit, in this case 0.2%.

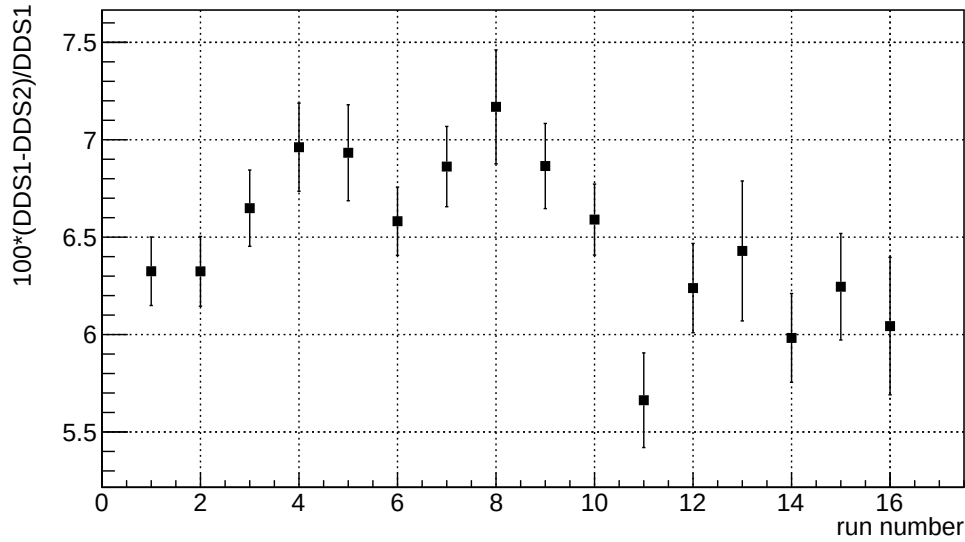


Figure A.9: Mean ratios of the two DDS detectors. Data points and uncertainties are obtained from mean and sigma of Gaussian distributions for each run (as shown for run 1 in figure A.8). A systematic difference in the order of 0.5% is observed between runs with carbon ions (runs 1-10) and protons (runs 11-16).

The algorithm to reverse the averaging of the current measurements with the PTW ionisation chamber is presented in the following: table A.6 shows the obtained raw and averaged currents if one assumes current measurements every 50 ms that give the raw currents A, B, C etc. and averaged currents called A', B', C' etc. It is possible to calculate the raw currents from the averaged currents with the formula presented in the last row of the table. The necessary assumption for this is that the first current measurement is 0. This is not true but the value for non-spill currents – that are the first values of each run – is negligible compared to those during spill and thus the formula can be applied.

Table A.6.: Raw and averaged currents.

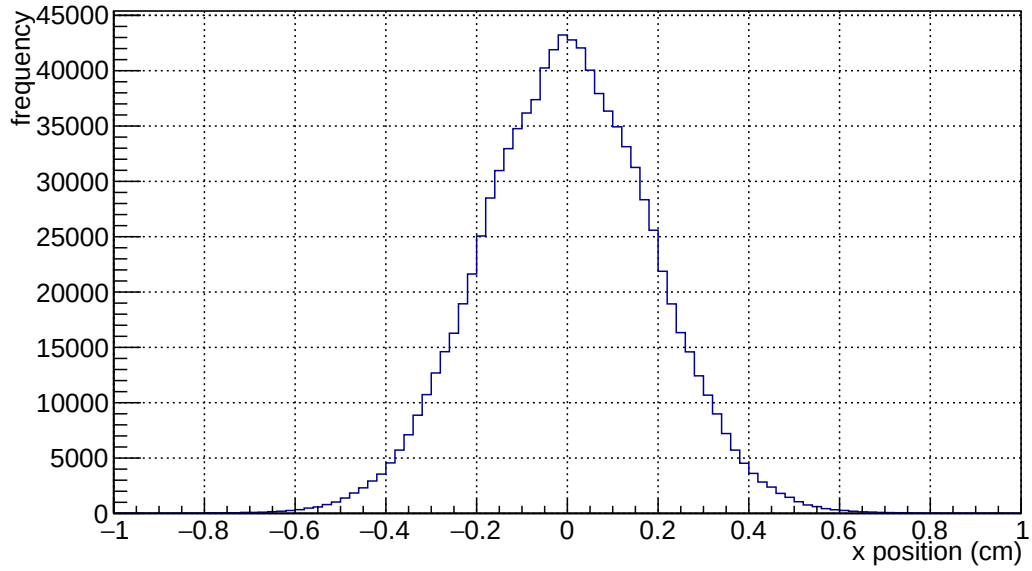
time (ms)	Raw current	Averaged current	Calculated raw current
50	$A = 0$	-	$A = 0$
100	$B \neq 0$	$A' = \frac{1}{2} (A + B) = \frac{B}{2}$	$B = 2A' - 0$
150	$C \neq 0$	$B' = \frac{1}{2} (B + C)$	$C = 2B' - B$
$n \cdot 50$	$I_{\text{raw}}(n)$	$I_{\text{average}}(n)$ $= \frac{1}{2} (I_{\text{raw}}(n-1) + I_{\text{raw}}(n))$	$I_{\text{raw}}(n)$ $= 2I_{\text{average}}(n) - I_{\text{raw}}(n-1)$

A.10. Additional FLUKA Results

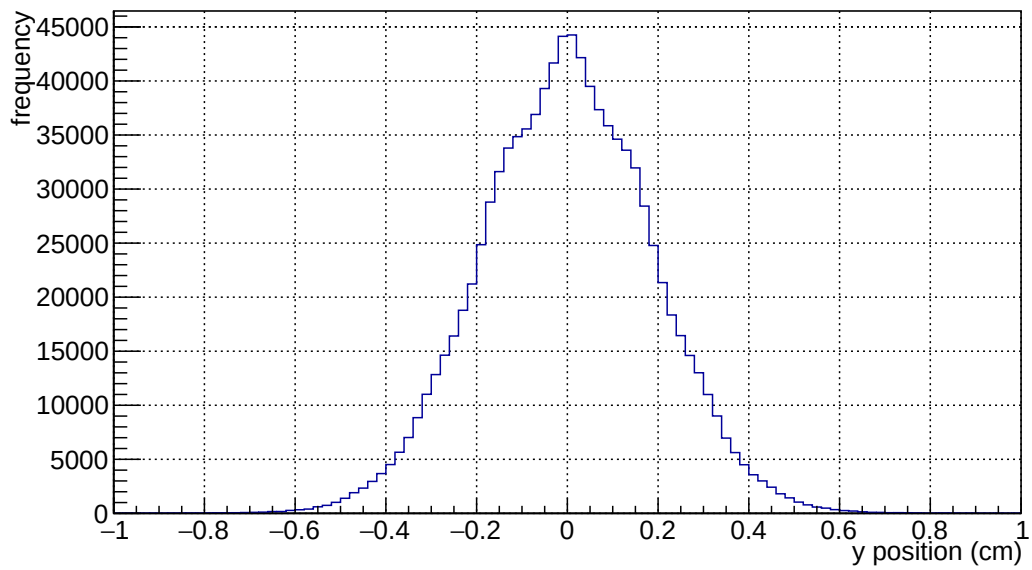
Figure A.10 shows the distribution of the x- and y-position of the carbon ions with an energy of about 3.3 GeV when leaving the beam nozzle at CNAO as simulated for the standard FLUKA simulation used at CNAO (see also section 5.6.1).

A.11. Summary of All CNAO Runs

Figure A.7 shows the beam and GEMPix settings of all completed runs performed with the integrated system at CNAO. Runs aborted for example due to obviously bad settings are excluded.



(a)



(b)

Figure A.10: Distributions of (a) the x-position and (b) the y-position of the carbon ions with an energy of about 3.3 GeV when leaving the beam nozzle.

Table A.7.: List of all runs performed with the integrated system at CNAO. The first digit of the run number encodes the number of the shift. If more than one run number is given per row, the given runs needed to be merged to obtain a complete depth scan.

Date	Run number	Particle	Range (mm H ₂ O)	Energy (MeV/u)	GEMPix gain (V)	GEMPix clock (MHz)	Frame Length (ms)	Remarks
17.09.17	109/110	C	150	280	960	2.4	20	
17.09.17	114/115	C	150	280	960	2.4	20	
17.09.17	116	C	250	380	960	2.4	20	
17.09.17	119/120	p	250	–	990	2.4	20	
26.11.17	207	C	150	280	950	2.4	20	
26.11.17	210/211	C	200	332	950	2.4	20	
26.11.17	213/214	C	150	280	950	2.4	20	
26.11.17	219/220	C	150	280	915	2.4	20	
26.11.17	221/222	C	200	332	915	2.4	20	
26.11.17	224	C	250	380	915	2.4	20	
26.11.17	225/226	C	250	380	915	2.4	20	
26.11.17	228/229	p	250	–	945	2.4	20	
05.04.18	–	C	150	280	990	–	–	Tests for signal evolution in the GEMs: turning on only selected electric fields of the GEMs
05.04.18	–	C	150	280	990	–	0.01	Tests with very short GEMPix frames
05.04.18	306/307	C	150	280	960	4.8	10	
13.05.18	403/404	C	150	280	990	4.8	10	

Table A.7.: List of all runs performed with the integrated system at CNAO (continued). The first digit of the run number encodes the number of the shift. If more than one run number is given per row, the given runs needed to be merged to obtain a complete depth scan.

Date	Run number	Particle	Range (mm H ₂ O)	Energy (MeV/u)	GEMPix gain (V)	GEMPix clock (MHz)	Frame Length (ms)	Remarks
13.05.18	–	C	150	280	–	–	–	Tests with ionisation chamber: different integration times
13.05.18	405/406/407	C	150	280	1010	4.8	10	
13.05.18	408/409	C	150	280	970	4.8	10	
13.05.18	410/411	C	150	280	1030	4.8	10	
13.05.18	413/414	C	200	332	990	4.8	10	
13.05.18	415/416	C	250	380	990	4.8	10	
13.05.18	420/421/422	p	250	–	990	4.8	10	

Acknowledgements

I would like to thank my supervisors Marco Silari (CERN) and Achim Stahl (RWTH Aachen University) for the opportunity to write this thesis and their support and comments. Marco Silari's and Fabrizio Murtas' help throughout the whole time at CERN was great.

The donation of the water phantom by the Luzerner Kantonsspital (LUKS) was a major contribution to the integrated system. Namely the help of Regina Seiler was simply perfect!

Concerning the ionisation chamber, I would like to thank Hamza Boukabache and Ciaran Toner for the test measurements with the CROME-pre-prototype. Their and Michel Pangallo's advice on the later acquired readout PTC IC101 and the cabling was very helpful. Furthermore I am grateful to Ali Day, Frederic Magnin and Suleyman Dinger who provided me with the proper cabling (i.e. the SPA6 cable and the adaptors). All of them are members of CERN HSE-RP-IL. The test measurements at CNAO were made possible by Mario Ciocca and Alfredo Mirandola. The discussions with Marco Donetti on the DDS were very fruitful.

Uncounted test measurements at the calibration laboratory were supported by Pierre Carbonez, Alix Chantelauze and Gilles Lagneau (CERN HSE-RP-DC).

The integrated system was set up and first tested at CERN's Ideasquare. Harri Toivonen's (CERN RCS-PRJ) help with the 3D printers was a huge support.

For the FLUKA simulation the help of Andrea Mairani (affiliated to CNAO and HIT) is very much appreciated as he provided the phase space files.

I would like to thank all colleagues from my section at CERN (HSE-RP-SP) for the discussions, their comments and their help.

Last but not least I would particularly like to thank my parents for their unlimited, perfect support!

This work has been sponsored by the Wolfgang Gentner Programme of the German Federal Ministry of Education and Research (grant no. 05E15CHA). Funding for the integrated system was granted by the CERN Medical Applications Project Forum (MAPF).

Eidesstattliche Erklärung

Ich, Johannes Leidner,

erkläre hiermit, dass diese Dissertation und die darin dargelegten Inhalte die eigenen sind und selbstständig, als Ergebnis der eigenen originären Forschung, generiert wurden.

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Acronyms

- ANDRA** Agence nationale pour la gestion des déchets radioactifs, French National Agency for Radioactive Waste Management. 61
- ASIC** Application-Specific Integrated Circuit. iii, v, vi, 1, 28, 30, 34–36, 38, 39, 43, 46, 88, 137, 138, 143, 146, 147, 190
- ATLAS** A Toroidal LHC ApparatuS, an LHC experiment. 36
- CERN** Organisation Européenne pour la Recherche Nucléaire, European Organization for Nuclear Research. iii, v, 1, 19, 21, 30, 59–62, 64, 69, 78, 96–99, 104, 105, 108, 109, 121, 122, 124–126, 128, 145, 147, 165, 190, 193, 194, 197, 199
- C.L.** confidence level. 72, 74–77
- CMOS** complementary metal–oxide–semiconductor. 30
- CMS** Compact Muon Solenoid, an LHC experiment. 28
- CNAO** Centro Nazionale di Adroterapia Oncologica, Italian National Centre of Oncological Hadrontherapy. 5, 9, 14, 18, 20, 26, 42–44, 47, 54, 79, 81–84, 86–91, 95, 99, 104, 111, 113–115, 117, 121, 122, 124–126, 128, 130, 131, 133, 134, 138, 140–142, 145, 146, 160, 162, 163, 165, 189, 192–194, 197, 198
- COMPASS** Common Muon and Proton Apparatus for Structure and Spectroscopy, a CERN experiment. 28
- CT** computed tomography. 85
- DDS** Dose Delivery System. 83, 88, 91–95, 113, 115–121, 130, 157–159, 165, 193–195
- DNA** deoxyribonucleic acid. 143
- DTM** Difficult-to-Measure. 60, 62, 78
- ETM** Easy-to-Measure. 60
- FLAIR** FLUKA Advanced Interface. 20

- FLUKA** FLUktuierende KAskade (Fluctuating Cascade). iii, v, 20, 61, 89, 94, 95, 121, 124, 128, 130, 131, 133, 141, 146, 160, 165, 194
- FPGA** Field Programmable Gate Array. 31
- FWHM** full width at half maximum. 41, 43, 83, 112, 114, 115, 190, 193
- GEM** Gas Electron Multiplier. iii, v, vi, 1, 16, 21–30, 36–41, 46, 50, 56, 57, 88, 93, 129, 130, 132, 134, 138–143, 146, 148, 150, 162, 189–191
- GUI** Graphical User Interface. 17, 18, 189
- HIT** Heidelberger Ionenstrahl-Therapiezentrum, Heidelberg Ion-Beam Therapy Center. 80, 81, 121, 122, 165
- HV** high voltage. 27, 37–40, 45–48, 50–53, 97, 98, 100, 101, 107–109, 113, 129, 145, 190, 191
- IAEA** International Atomic Energy Agency. 59, 60, 80
- ILC** International Linear Collider. 28
- INFN** Istituto Nazionale di Fisica Nucleare, Italian National Institute for Nuclear Physics. 39
- InGaN** indium gallium nitride. 54
- IRAS** Indice Radiologique d’Acceptation en Stockage, hazard factor. 61
- ISR** Intersecting Storage Rings. 59
- ISS** International Space Station. 36
- KN** Key Nuclide. 60
- LabVIEW** Laboratory Virtual Instrument Engineering Workbench. 20, 39, 40, 100, 101, 117, 190, 193
- LED** light-emitting diode. 54–57, 191
- LEP** Large Electron-Positron Collider. 60, 61, 69
- LHC** Large Hadron Collider. 1, 24, 59, 98, 199, 200
- LHCb** Large Hadron Collider Beauty, an LHC experiment. 24, 28
- LINAC** linear accelerator. 80, 82, 84

LV low voltage. 46, 47, 98

MAFalda Medipix Analysis Framework. 18, 19, 189

MICROMEGAS MICRO-MESh Gaseous Structure. 21

MIT Marburger Ionenstrahl-Therapiezentrum, Marburg Ion-Beam Therapy Center. 80, 81

MWPC Multi-Wire Proportional Counter. 21, 25

Nikhef Nationaal Instituut voor Kernfysica en Hoge-Energiefysica, Dutch National Institute for Nuclear and High Energy Physics. 39

NIST United States National Institute of Standards and Technology. 7, 11, 13, 38, 62, 65

PC Personal Computer. 31, 39, 97

PMMA Poly(methyl methacrylate). 89, 155

PTC Pyramid Technical Consultants. 98, 105, 113, 115, 121, 155, 156, 165, 193, 198

PTW Physikalisch-Technische Werkstätten Dr. Pöchlau GmbH. 85, 87–89, 92–95, 97, 98, 105, 113–121, 124, 126, 154, 160, 192–194, 197

RBE relative biological effectiveness. 80, 143

RF radiofrequency. 60, 61, 69, 82

SEU Single Event Upset. 35

SOBP Spread-Out Bragg Peak. 81

TEPC tissue equivalent proportional counter. 143

TFA very-low-level activity, très faible activité. 60, 61

TOA Time-of-Arrival. 31, 32, 55

TOT Time-over-Threshold. 31–35, 41–45, 48–53, 66, 67, 92, 104, 140, 148, 150, 190, 191, 195

TPC Time Projection Chamber. 24, 28, 39

TREC Traceability of Radioactive Equipment at CERN. 69

TTL transistor-transistor logic. 31, 98

USB Universal Serial Bus. 31, 39, 98

UV ultraviolet. 54–57, 150, 191

voxel volume pixel. 82, 85