Proton Radiography with a Timepix3 based Gaseous Tracking Detector

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Detector Research and Development
Nikhef

September 2015
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Abstract

Proton radiography is used as a tool to improve the treatment plans of proton therapy. In this technique, the phantom under investigation is irradiated by protons. If the position and direction of the protons are determined before and after the phantom together with a measurement of the residual energy, an image of the phantom can be reconstructed. In this analysis the renewed proton radiography set-up, used at Nikhef is presented. Two GEM-based time projection chambers, with a Timepix3 quadboard as basis are used for the proton tracking, while a BaF$_2$ crystal is used for the residual energy measurement. With this set-up, measurements have been done with a proton rate up to 10 kHz, made possible by the implementation of the Timepix3 chips with their data-driven and zero-suppressed readout architectures. Also, a study on the response of the BaF$_2$ calorimeter was performed in order to deal with the high proton flux. Furthermore, a study on the performance of the tracking detectors is presented. It was found that the angular resolutions are 30.7 mrad and 23.4 mrad in the $xy$ and $zy$ plane respectively, which are dominated by the clustering effect of the triple-GEM structure and the inhomogeneous electric field in the drift region. The low angular resolution impedes an appropriate calculation of the entry and exit locations of the protons on the phantom. However, energy-loss radiographs are presented without the use of the angular information.
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**Abstract**

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Chapter 1

Introduction

In high energy physics experiments, like those performed at the LHC collider at CERN, proton-proton collisions are used in order to investigate particle interactions in the Standard Model and beyond. Knowledge and technology that scientists have gained doing such challenging experiments are used in many other fields outside the physics community. Medicine is one of the most interesting fields where this happens, since the most fundamental principles of physics are used in order to better understand certain diseases and provide health care treatments.

Since the early 20th century it has been known that ionizing radiation has the potential to damage cells. In recent decades, there has been a growing interest in performing this operation using protons [1], which has potential advantages over the conventional X-ray irradiation. Protons are preferred mostly because the greatest radiation dose occurs only in the last 10% of the proton range, known as the Bragg peak [2]. In this way the highest dose can be concentrated in the tumor and the dose in healthy tissue can be minimized.

In order to deposit the dose exactly where the tumor is located, accurate information is needed about where the proton will most likely lose its energy while traversing the tissue. This requires a 3D map of the relative proton stopping power of the body under treatment. The conventional method of translating the Hounsfield units (i.e. units of X-ray attenuation used in conventional X-ray Computed Tomography) to relative proton stopping power values introduces a calibration uncertainty that can result into an error of about 4% for deep seated tumours [3, 4].

In the early 60s the concept of using protons for medical imaging was developed [5]. By measuring the direction of the incoming and the outgoing single protons and simultaneously measuring the deposited energy, an image can be reconstructed of the phantom under investigation. Proton imaging has the great advantage that both treatment and diagnosis are performed with protons and the conversion for the treatment plan is therefore more accurate. However, protons are highly subject to multiple Coulomb scattering and thus affect the spatial resolution of the relative stopping power map. Only in the last
decade, with the growing number of medical proton accelerators, considerable progress has been made in this promising technique [6, 7].

A relative proton stopping power map can be obtained in several ways. We can distinguish them into two main categories: proton energy-loss radiography and proton scattering radiography. In the first scenario the energy loss of single protons is connected to the location of the phantom where the protons came from. The stopping power across the whole phantom can then be determined. For this method the determination of the entrance and exit location of the protons is extremely important together with the energy loss measurement. However, since the stopping power depends mainly on Z/A, which for most soft tissues in the human body is practically identical, the resulting images will be of low contrast [6].

In the second scenario of proton scattering radiography, the scattering angle is obtained by measuring the entrance and exit angle of the single protons and the difference between them is then assigned to the corresponding location on the phantom. With this method, information on the proton scattering power is obtained, which is inversely proportional to the stopping power of the traversed material [6]. Compared to the proton energy-loss radiography, additional information of the entrance and exit angles are needed. The scattering angles are expected to range from 5 mrad in 5 cm of water up to 25 mrad in typical bones of the human body [8, 9].

For both categories a better approximation is obtained by calculating the most likely path of the protons inside the phantom in order to account for the different materials that a proton traversed. Finally, a tomography scan can be reconstructed either from energy-loss or scattering radiographs for three-dimensional insights.

There are a number of possible set-ups to perform proton radiography. Most of these proton imaging set-ups are based on silicon detectors [10–12]. In 2011, a first proof of principle of a gaseous Time Projection Chamber set-up, based on the Timepix chips [13], was performed successfully [14]. Gaseous detectors employed as 3D particle trackers have the advantage over solid state detectors that they are radiation hard and have low interference with the proton beam. An advanced study, subsequent to this first proof of principle, has been performed by [15] and [16], with even better results.

Unfortunately, two of the major problems of the previous set-up remain unsolved: (i) the low proton rate that the current set-up can handle and (ii) the inaccuracy of the determination of the three-dimensional track, specially the angular information of the track.

It is shown by [16] that in order to produce a radiograph consisting of $0.5 \times 0.5 \text{ mm}^2$ bins, one needs to reconstruct at least $8000 \text{ protons/cm}^2$. Currently a proton rate of $50 \text{ Hz}$ can be handled, which implies an exposure time of 13 hours for a $20 \times 20 \text{ cm}^2$ radiograph, while a typical radiograph takes $\sim 0.04 \text{ sec}$. An improvement in this aspect is obviously needed.
Moreover, the angular uncertainties of the reconstructed tracks are above the 5 to 30 mrad depending on the plane. The above mentioned scattering angles between 5 and 25 mrad could not reliably be observed with the current detector accuracy. For proton scattering radiography, the angular uncertainties should be well below 1 mrad [6].

In order to solve these two major obstacles, the current study provides a redesign of the set-up with some minor and major changes. The most important improvement is the implementation of the Timepix3 chip [17] in the tracking detectors. This chip has the characteristics that it can handle $\sim$80M hits per second using a data-driven and zero-suppressed readout system and that both Time over Threshold and Time of Arrival can be measured simultaneously, providing a better measurement of the z-component of the tracks. Furthermore, a fast oscillator with 1.56 ns resolution is implemented in order to provide a better Time of Arrival measurement. The increased time resolution from 10 ns to 1.56 ns is used for a more reliable and precise track reconstruction. Furthermore, detailed studies were performed on the energy measurement, the electric field inside the Time Projection Chamber, on the electron multiplication based on Gas Electron Multiplier foils [18] and on the final performance of the Time Projection Chambers.
Chapter 2

Particle Interactions in Medicine

2.1 Radiation Therapy

The interest in proton radiography originates from the possibility of destroying tumors by irradiating them with protons, which is called proton therapy. The idea to kill tumor cells by means of irradiation has its origins back in 1920. X-ray photons were first used to penetrate into the human body and damage the DNA of the tumor cells. The interaction between the radiation and the tissue occurs via nuclear and atomic interactions. In these interactions, secondary particles can be created that deposit energy along their path. This deposited energy is called dose and is measured in Gray. The deposited dose can lead to DNA double strand break, which can eventually result into mutation or even death of the cell. Ideally, all the dose is deposited into the cancerous tissue and healthy tissue is preserved from the irradiation. For several reasons such as uncertainties in location of the target volume, movements of the patient and the fact that the irradiating beam needs to penetrate first through the healthy tissue, the deposited dose to the healthy tissue will always be non-zero.

![Graph showing the relative dose as a function of the distance in water for protons, photons, electrons, and carbon-isotopes.](image-url)

Figure 2.1 – Relative dose as function of the distance in water for protons, photons, electrons and carbon-isotopes. Image courtesy of N. van der Weiden.
The most developed irradiation techniques at the moment make use of photons or electrons. Figure 2.1 shows the relative dose delivered as a function of the distance in water for various particles used in radiotherapy. For X-rays, the dose arises from the fact that the photons ionizes the matter, liberating electrons that can subsequently damage the tissue. The graph shows that the dose for X-rays has a short build-up region, due to the short range that the electrons travel after ionization, and then decreases exponentially. This means that a higher dose delivery to the tumor compared to the healthy tissue can only be accomplished by irradiating the target volume from multiple directions. Summing up the beams from all directions will make the irradiated part outside the target volume significantly lower compared to the crossing of the beams.

In contrast to photons, the energy deposition of charged, heavy particles is inversely proportional to the distance in the tissue. The mean rate of energy loss by moderately relativistic charged heavy particles is well-described, up to a few percent, by the Bethe-Bloch equation [19]:

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

where the symbol definition are given in Table 2.1.

**Table 2.1** – Definition of the variables used in Eq. 2.1.

<table>
<thead>
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<th>Symbol</th>
<th>Definition</th>
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<tr>
<td>$\beta$</td>
<td>$\frac{v}{c}$</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>$\frac{1}{\sqrt{1-\beta^2}}$</td>
</tr>
<tr>
<td>$K$</td>
<td>$4\pi N A r_e^2 m_e c^2 = 0.307$ MeV mol$^{-1}$ cm$^2$</td>
</tr>
<tr>
<td>$A$</td>
<td>atomic mass</td>
</tr>
<tr>
<td>$z$</td>
<td>charge number of incident particle</td>
</tr>
<tr>
<td>$Z$</td>
<td>atomic number of the absorber</td>
</tr>
<tr>
<td>$m_e c^2$</td>
<td>the electron mass (0.511 MeV)</td>
</tr>
<tr>
<td>$T_{max}$</td>
<td>maximum kinetic energy which can be imparted to a free electron (MeV)</td>
</tr>
<tr>
<td>$I$</td>
<td>mean excitation energy (MeV)</td>
</tr>
<tr>
<td>$\delta(\beta \gamma)$</td>
<td>density effect correction to ionization energy loss</td>
</tr>
</tbody>
</table>

Figure 2.2 shows the evolution of Eq. 2.1 for protons in liquid water [9]. Protons with an initial energy of 200 MeV lose only a few MeV in the first centimeters. The energy loss grows exponentially with decreasing energy and results therefore in an abrupt energy deposition at a specific depth, the “Bragg peak”. After the Bragg peak the protons are...
stopped and will therefore not affect the tissue anymore. In fact 50% of the total proton energy could be concentrated in a few centimeters. This makes protons good candidates for irradiation therapy, since the dose is very localized.

The depth of the Bragg peak depends on the energy of the incoming proton and on the density of the traversed material: the higher the energy the further the proton will penetrate into the tissue. This effect is shown in Figure 2.3 for several proton energies in water [20]. As Figure 2.1 shows, this holds also for other charged particles like $^{12}$C.

The idea of using fast protons for radiological purposes was first proposed in 1946 by Robert Wilson [21]. With the availability of new proton accelerators at energies up to 400 MeV, the high penetration depth of protons was exploited. It was pointed out that protons of 200 MeV for example, could penetrate 27 cm into tissue and were therefore excellent candidates for radiological purposes as at that energy they would completely traverse the patient.

It should be remarked that the transversal diffusion of protons is higher than for photons, due to multiple Coulomb scattering. Depending on the location it could be a disadvantage compared to X-ray beams.

Nevertheless, treatment plan comparisons show that in the majority of the cases the dose delivered to the healthy tissue using photons will be twice as much as treatments that make use of protons [23]. Especially for smaller volumes or organs located at critical positions such as the spinal cord the advantage of protons is remarkable.

![Figure 2.2](image)

Figure 2.2 – Bethe-Bloch equation for protons in water from NIST. The Proton Therapy domain is from 50 keV to 200 MeV and the Proton Radiography domain ranges between the 200 MeV and the Minimum Ionizing Particle scale.
2.2 Imaging

When a patient is treated with protons, the Bragg peak must be located at the depth of the tumor with high accuracy. In order to tune the proton beam at the right energy, the Relative Stopping Power (RSP) of the traversed medium should be known. Due to the localized behaviour of the Bragg peak, a small uncertainty could harm the patient considerably. Currently, imaging techniques such as MRI, X-ray CT, PET or ultrasounds are used to determine the location of the tumor. For more information on these techniques and applications in proton therapy see [25]. These techniques offer a high resolution image of the location of the tumor. Although various algorithms have been developed over the years in order to estimate the RSP for proton treatments on the basis of these images, the conversion between the image and the treatment plan leads to uncertainties up to 4% [4]. Furthermore, uncertainties arise from the fact that the position of the tumor may change when the patient is moved from the imaging location to the proton beam. Many techniques are investigated in order to reduce these uncertainties [27-29]. In this study proton radiography is discussed, in which protons themselves are used to produce radiographs that could be converted into RSP maps and used for treatment plans, introducing smaller conversion uncertainties.
2.3 Proton Radiography

The basic idea of proton radiography is to have high energy protons travel through the patient in such a way that the Bragg-peak is located well outside the body and have a minimal dose deposition inside the patient. When a proton penetrates through the patient it will interact with the tissue. In this process it will scatter and lose a certain amount of energy, depending on the characteristics of the matter it encounters. If one is able to determine the path of the single protons and measure the deposited energy, both scattering and energy-loss radiographs can be reconstructed of the irradiated area.

This technique was first formulated in 1963 by A.M. Cormack \[22, 23\]. He proposed “...the determination of a variable density of matter with constant chemical composition, using the energy loss of charged particles in the matter.”. Only in 1972 Goitein performed the first tomographycal reconstruction with heavy charged particles (alpha particles) \[24\]. In 1976 the first prototype of proton Computed Tomography (pCT) was constructed by Cormack and Koehler \[25\]. With this proof of principle they showed that density differences of 0.5% could be characterized. However, the presence of reconstruction artefacts was pointed out at the boundaries between different materials. This is due to the different ways in which the protons are subjected to multiple Coulomb scattering in the different absorber materials.

Later, proton radiographs were published measuring the residual energy and exit position of the single protons, increasing the reliability of the images \[26–28\]. With these first results it was shown that a pCT scanner could be developed, delivering a similar dose as an X-ray CT; however, disadvantages raised from the lack of spatial resolution and the high costs of a proton accelerator. For these reasons pCT lost popularity for several years. A renewed interest in pCT came with the increase of the number of proton therapy centers in the 90’s, since proton therapy in combination with pCT results to be potentially less harmful.

2.3.1 Current Status of Proton Radiography

The general set-up for proton radiography consists of a proton beam providing protons with an accurate energy of 250 MeV, a tracking system before and after the sample and an energy sensitive device for a precise measurement of the residual energy. Figure 2.4 shows this principle schematically. After having measured the incoming direction, the outgoing direction and the residual energy of the single protons a most likely path (MLP) reconstruction algorithm could be applied in order to obtain the RSP map \[29–31\]. The MLP is calculated analytically for charged particles traversing a medium, subjected to multiple Coulomb scattering, when the entrance and exit positions and angles are defined. Effects of energy loss due to ionization are taken into account.

In the last decades, different techniques for proton radiography have been investigated.
Figure 2.4 – Basic set-up for proton radiography. Two sensitive proton tracking modules are positioned pre- and post-patient. A calorimeter is placed behind the trackers for the residual energy measurement.

In Italy, a silicon micro-strip tracker in combination with a segmented crystal calorimeter is under investigation. This set-up provides a high track resolution with >MHz proton rate handling; however, its high material density decreases the image resolution [11]. Similarly, the Loma Linda University Medical Centre (LLUMC) is constructing a detector based on a four-plane silicon track position measurement, followed by a calorimeter [10, 32–34].

A different system, based on nuclear emulsion detectors is under investigation [35]. Nuclear emulsion detectors are well known for the most accurate position measurements but have the disadvantage of long readout times. However, recent developments in fast automated scanning analysis systems allow for a high proton rate and make this research very interesting.

Another project was conducted at the Paul Scherrer Institute to perform proton radiography for position verification [36]. The system consists of two scintillating fibre hodoscopes and a range telescope made of plastic scintillator tiles and is capable of detecting position and range of $10^6$ protons/s and reconstruct images with a spatial resolution of $\sim 1 \text{ mm}$.

Furthermore, a system based on multiple position-sensitive Gas Electron Multiplier (GEM) detectors in the transversal direction for the proton tracking and a scintillator stack for assessing the proton residual energy is under investigation [37].

Finally, at Nikhef work has been done on a prototype that performs the tracking with gaseous Time Projection Chambers (TPC), based on GridPix charge sensitive chip detectors [14–16]. In the next chapters, the latest developments on this set-up will be described and characterized in detail. The main advantages of using gaseous TPCs are that they are radiation hard and have low interference with the proton beam.
Chapter 3

Proton Radiography Set-up

Currently, proton radiography at Nikhef is performed using the set-up shown in Figure 3.1. The proton beam passes through a thin scintillator and a TPC, then encounters the sample, a second TPC and finally the BaF$_2$ crystal for the energy measurement. Both the scintillator and the BaF$_2$ crystal produce scintillating signals at the passing of a proton. The coincidence between the two signals is used to produce an acquisition window for the TPCs. In this chapter a detailed description of these various components of the set-up is given.

![Figure 3.1 – Overview of the proton radiography set-up at Nikhef. From left to right there is a scintillator, the first TPC, the phantom, a second TPC and the calorimeter.](image-url)
Chapter 3. Proton Radiography Set-up

3.1 Time Projection Chamber

In order to measure the position and direction of the incoming and outgoing protons, a tracking detector is needed. As pointed out in Chapter 2, a gaseous TPC is used for this purpose in the current study. With this detector the proton tracks can be observed. Figure 3.2 shows the schematics of a TPC. As almost any detector, it consists of a sensing part, where the signal is produced and a signal processing part, where the useful information is extracted. The sensing part consists of a gas volume where the following important processes happen when a proton passes:

- ionization of the gas molecules
- liberated electrons drift toward the anode
- electron multiplication
- charge collection at the anode level

At the bottom of the gas volume, a pixelated charge sensitive device detects the multipliclated signal from the drifted electrons. The pixel-ID contains the x and y information of the interaction points. A measurement of the arrival time of the electrons in combination with a reference timestamp provide the z-position of the interaction point by this simple relation:

\[ z = (T_{\text{Arrival}} - T_{\text{reference}}) \times v_D, \quad (3.1) \]

where \( v_D \) is the constant drift velocity. In the current set-up the reference timestamp is given by the trigger signal.

3.1.1 Drift volume

When a proton passes through the gas volume there is a possibility that it ionizes the gas molecules. The interaction between the gas atom \( X \) and the proton \( p \) can be described as following:

\[ X + p \rightarrow X^+ + e^- \quad (3.2) \]

The probability for this process to happen depends on the choice of the gas and on the energy of the incoming particle. In this process the proton will lose a certain energy
given by Eq. 2.1 and its trajectory will change by the scattering angle $\theta_0$, given by:

$$\theta_0 = \frac{13.6 \text{MeV}}{\beta pc} z \sqrt{\frac{x}{X_0}} \left[ 1 + 0.038 \ln \left( \frac{x}{X_0} \right) \right]. \quad (3.3)$$

Here $p$, $\beta c$ and $z$ are the momentum, velocity, and charge number of the incident particle, and $x/X_0$ is the thickness of the scattering medium in radiation lengths.

After the ionization, the liberated electron has to reach the signal processing unit where the information of the location of ionization will be determined. On the top and the bottom of the gas volume a cathode and an anode are placed respectively, such that the free electrons are pushed towards the anode. If the electrons would drift in vacuum, they would accelerate up to high velocities and reach the anode in a short period. Due to the presence of the gas molecules the electron will scatter in all directions, but mostly in the preferred direction of the electric field. The net effect is that they will drift with a constant velocity $v_D$ and diffuse both in longitudinal and transversal direction. In the ideal drift volume we would like to have an as high as possible drift velocity for a fast position determination and minimal diffusion for low position uncertainties. In Figure 3.3 the drift velocity as function of the electric field is plotted for three commonly used gasses. Figure 3.4a and 3.4b show the longitudinal and transversal diffusion respectively as function of the electric field. In this study it has been chosen to use the gas mixture CO$_2$ArCF$_4$. This mixture is shown to perform well with a similar set-up at the GEMPIX collaboration [38]. From Figure 3.3, 3.4a and 3.4b we would deduce that the electric field should be chosen as high as possible. However, an excessive electric field in the drift region will accelerate the electrons in such a way that they ionize the gas further. These secondary electrons will produce a signal themselves, which reduces the accuracy of the position reconstruction. For the chosen gas mixture this happens with an electric field higher than 1000 V/mm. In the extreme case this will lead to breakdown, which makes the detector unreliable.

In the current study an electric field of 300 V/cm is chosen. This leads to a relative low drift velocity of 1 cm/$\mu$s, but it is shown from studies of the GEMPIX group that this is the optimal field strength for a GEM based detector. The resulting drift velocity is 1 cm/$\mu$s, with longitudinal and transversal diffusion coefficients of 0.0148 cm/cm and 0.0147 cm/cm respectively.

### 3.1.2 Electron multiplication

A typical pixelated charge sensitive device is not able to detect single electrons. The typical noise level is roughly of 100 electrons for each pixel. An electron multiplication step should be introduced for this reason. In order to describe this process we should introduce a parameter $\alpha$ called Townsend coefficient. Given a single electron in a region
Proton Radiography Set-up

Figure 3.3 – Drift velocity as function of the electric field inside the drift volume.

Figure 3.4 – Longitudinal (left) and transversal (right) diffusion coefficients (cm for 1 cm) for the three gasses as function of the electric field (V/cm).

of constant electric field, the electron gain for a certain distance \( x \) is given by

\[
G(x) = e^{\alpha x}
\]

and is an intrinsic property of the gas mixture in the drift volume. It is experimentally known that if \( \alpha x > 20 \) sparks are created that make the detector unstable.

If the gain is higher than 1, the secondary electrons could ionize the gas further, thus leading to avalanche creation. Many techniques, such as GridPix, micromegas and GEM foils are available for this process. Most of them; however, need post-processing of the chip, such as protection layers or the placing of a delicate grid on top of the chip. Gas Electron Multipliers (GEMs) have the advantage that a bare chip suffices. For this reason in this project, we chose to make use of GEM foils. Figure 3.5a shows a schematic
view of a single GEM foil. A 50 µm capton foil is enclosed between two thin copper foils. This sandwich structure is perforated every 140 µm. Between the two copper layers a potential difference of 8000 V/mm is applied, such that when an electron passes through the holes, an avalanche is created. In a typical GEM-based drift chamber three GEM foils are used. With such a structure a gain up to $10^6$ electrons could be achieved. Figure 3.5b shows the working principle of a triple-GEM structure. A dedicated control system unit has been developed for this system in order to provide a stable electric field inside the single GEMs and between the three GEMs [39]. The drawback of such a triple-GEM structure is that a single ionization will produce a signal spread over many pixels. This could have two effects: the accuracy of the determination of the location of the primary electron may decrease and many hits can overload the readout device.

![Figure 3.5](image)

**Figure 3.5** – Single GEM foil (left) consisting of a capton layer enclosed between two thin copper layers. The foil is perforated such that the electrons can pass and avalanches are created. Triple GEM structure for electron multiplication (right).

### 3.1.3 Electric field

The distance between the first GEM foil and the cathode is chosen to be 50 mm, which is 20 mm higher than the previous set-up in order to go towards a larger device for clinical purposes. In this configuration, the approximation of the infinite parallel plate will not hold. At the borders of the drift chamber the electric field will suffer from inhomogeneities. This effect is shown in Figure 3.6a, where the field strength is plotted as function of the position inside the chamber. In order to prevent this effect, a field cage is designed. This cage consists of a cathode on the top, the grounded chipboard at the bottom and capton foil as walls. The capton foil is tested to be gas-tight for the use in gaseous detectors. It is a 50 µm thick foil, with 0.5 mm wide copper strips every millimeter. The strips are connected by a resistive chain with resistors of 10 MΩ. A finite element simulation of the electric field in this configuration has been carried out in Elmer and Garfield [40, 41]. The result is shown in Figure 3.6b. The field cage is shown, with the respective metallic strips. The colors represent the electric potential. In this
simulation the anode has a potential of 0 V and the cathode 5000 V. It is shown that inside the field cage the electric potential is equal at a constant height. This means that the electric field in the z-direction is homogeneous. This is of crucial importance for the operation of the TPC, since the electron path will not be distorted. The homogeneity of the electric field will be further discussed in the chapter on detector performance.

![Electric Potential Simulation](image)

**Figure 3.6** – Electric field simulation of the drift chamber without drift cage (a) and including the drift cage (b).

### 3.1.4 Timepix3 Chip

Once the avalanche has been produced, one needs to collect the signal and process it to obtain the needed information. A charge sensitive pixelated device that is able to measure the time of arrival of the electrons is needed. The Timepix3 chip is used for this end [17]. This chip is the successor of the Timepix chip, one of the chips developed in the Medipix family. The Timepix3 chip consists of 256x256 square pixels of 55 µm side length, which makes the Timepix3 chip competitive with most of the existing imaging devices in terms of spatial resolution.

![Frontend Electronics Block Diagram](image)

**Figure 3.7** – Basic blocks which constitute the frontend electronics of a typical chip used for the readout of particle detectors.

Figure 3.7 shows the basic blocks which constitute the frontend of the chip. The signal
produced by the avalanche is collected on the input pad and amplified by a charge sensitive amplifier. After this stage the signal is shaped in order to transform the very fast input signal into a more easily processable shape. Furthermore, at the shaping stage, the signal is filtered in order to produce a better signal to noise ratio. When the shaping is performed, the signal is compared to an externally set threshold. If the result is positive, the presence of a pulse is recorded. The output of the discriminator is a linear function of the input pulse and is further processed.

Figure 3.8 – Timing diagram of the digital processing per pixel.

Figure 3.8 shows the timing diagram of the digital processing. At the pixel level a 40 MHz system clock is continuously counting. When the output of the discriminator is positive, a faster oscillator (640 MHz) starts to count until the first rising edge of the system clock. The number of counts of the fast oscillator is registered together with the timestamp of the rising edge of the system clock (Time of Arrival) and the number of clock cycles that the signal remained over threshold (Time over Threshold). All this can happen without dead-time if the rate is below 20 Mhits/s/cm², due to a data-driven and zero-suppressed readout.

For the signal to reach threshold it takes a certain time. This rise time depends strongly on the incoming charge. Large charge signals will reach the threshold earlier than signals with small charge signals. This results into a charge dependency of the Time of Arrival, as shown in Figure 3.9. This intrinsic electronical effect is called timewalk.

Fortunately, there is a method to correct for the timewalk. The Timepix3 chip is able to measure both Time over Threshold and Time of Arrival. Since the timewalk depends on the charge, it could be parameterized using the Time over Threshold information, which is proportional to the charge [42]. This parameterization is finally used to correct the Time of Arrival for the timewalk effect.

Furthermore, the shape of the amplified signal depends on many intrinsic characteristics and externally controllable parameters. An important variable is the Krummenacher
Chapter 3. Proton Radiography Set-up

Figure 3.9 – The signal of two hits with different charge. Low charge corresponds to little ToT counts and long timewalk \( t_w \) (lower line). High charge leads to many ToT counts and short timewalk (upper line).

current, \( I_{Krum} \). This parameter influences the decay time of the signal. A low value of \( I_{Krum} \) means that the falling time of the signal is long which makes the dead-time of the pixel longer. Furthermore, the long tail of the signal will have strong fluctuations resulting in a bad signal to noise ratio. However, a high value of \( I_{Krum} \) results into a short falling time. The Time over Threshold is then reduced, but will be more sensitive to noise. In the measurements performed in this study a compromise is found and \( I_{Krum} \) is set to 1.8 nA.

After the pixel settings are set, the threshold of each individual pixel should be calibrated. A threshold equalisation procedure is therefore performed. The result is an almost homogeneous hitmap of the total chip, as shown in Figure 3.10. An empty region is visible at the border of the chip, due to misalignment of the GEM foils. Furthermore, non working pixels are identified such that at acquisition time they are not read out.

3.2 Timepix3 Readout

The TPCs are designed with a basis of \( 2 \times 2 \) Timepix3 chips, for a total electron collection area of \( 3 \times 3 \) cm\(^2\). The four chips are mounted on a quadboard, connected by wirebondings (see Figure 3.11).

To exploit the performance of the Timepix3 chips, a state of the art readout system is required. The signals are transmitted through the wirebondings to the quadboard that is read out through 12 links by a readout system called SPIDR. This system is
able to collect, elaborate and send 80 Mhits/chip/s through a 10 Gbit ethernet connection. Moreover, the SPIDR system has three external inputs: the shutter to define an acquisition window, an external clock as reference clock and an independent trigger that will give the $T_{\text{reference}}$ of Eq. 3.1.

A dedicated data acquisition program is written in order to obtain the right information at the right time from the Timepix3 chip. When a run starts, firstly the chips need to be restored to the user defined parameters. A general reset is therefore performed. After this reset, the shutter can be opened and the hit information is extracted. Since there is limited space reserved for the timing information, the system clocks on the chip have a temporal range of only a few microseconds. For this reason, at the SPIDR level, an additional counter is introduced: the SPIDR time. Introducing this counter, acquisition times of $\sim 28$ seconds can be recorded without repetition. Additionally, the SPIDR system is able to measure the arrival time of an external input trigger. At the end of the run, the shutter is closed and the acquisition terminates. In addition, a cooling system is designed to obtain a stable acquisition temperature of $40 \pm 0.2 \, ^\circ C$.

### 3.3 Residual Energy Measurement

Once the protons have passed the phantom and the tracking detectors, the residual energy of the single protons needs to be measured. A BaF$_2$ crystal coupled to a Photon Multiplier Tube (PMT) is used for this purpose. Figure 3.12 shows a picture of this
apparatus.

![Figure 3.12 – Structure containing BaF$_2$ crystal and the corresponding PMT for the residual energy measurement.](image)

3.3.1 BaF$_2$ Crystal

If a proton enters the crystal, it excites the BaF$_2$ molecules, which emit scintillating light when decaying back to their ground state. The amount of produced light is proportional to the deposited energy in the crystal. BaF$_2$ has two main excited states producing two signals with different wavelengths ($\lambda = 195$ nm and $\lambda \sim 320$ nm). It has been established that the ratio of both contributions remains constant over the full dynamic range up to relativistic and even ultra-relativistic proton energies [43]. Therefore, when a proton enters the crystal, scintillation light is produced and can be distinguished into two signals. These two signals are captured by the PMT and transmitted to the readout system as analog signals. A typical event of an incoming muon is shown in Figure 3.13 after digitization, with the output voltage as function of the time. A clear distinction in time is visible between the two signals. We will refer to the red signal as the short signal and the green as the slow signal. Since the ratio of the production of the two signals is proven to be constant, one can consider to use only one out of the two signals for the residual energy measurement. As can also be seen from Figure 3.13, the slow signal has a higher signal to noise ratio, which makes it a better candidate for a precise energy measurement. This pulse takes almost 10 µs, which means that a proton rate of 10 kHz could be achieved with ~10% pile-up. The short signal is used in combination with the first scintillator to produce a trigger for the acquisition systems.

The deposited energy in the sample can then be calculated subtracting the deposited energy in the crystal from the initial beam energy. This is only valid if the protons are completely absorbed in the crystal, since only then the total residual energy is measured. Figure 3.14b shows a simulation of the energy deposition of 150 MeV protons in the BaF$_2$ crystal as function of the depth. At a depth of 60 mm no interaction takes
place anymore. Besides, Figure 3.14a shows the transversal diffusion in the crystal. A diffusion of 0.4 cm/cm is calculated. The crystal used in this study has a depth of 30 cm and a radius of 7 cm and is therefore well dimensioned to stop all incoming protons, considering a beam diameter of 5 cm.

![BF2 Crystal](image1)

![Edep (MeV/mm) along BaF2 crystal](image2)

**Figure 3.14** – Simulation of 150 MeV protons through a BaF$_2$ crystal (a). Normalized energy deposition of 150 MeV protons along the length of the BaF$_2$ crystal (b).

A calibration curve needs to be used in order to relate the output voltage of the slow signal to a given energy. The expected energy ranges from the full beam energy (150 MeV)
to total absorption (0 MeV). In order to obtain the energy of the protons the total amount of produced light should be integrated; however, previous searches show that the energy of the protons is also proportional to the peak-voltage of the slow signal [16]. Therefore, also in this study the peak-voltage of the slow signal will be used for the energy determination.

### 3.3.2 Digitization of the Signal

After the scintillating signal is collected in the PMT, it must be recorded and stored. For this purpose a 250 MSamples/s Caen digitizer is used. The fast-ADC board provides continuous 12 bit sampling of the signal without dead-time. There are 1024 capacitors that collect the charge proportional to the input signal. With a 250 MHz sampling rate, this corresponds to a 4\(\mu\)s temporal window. Using an usb-interface, an event rate of 30 kHz could be reached, limited by the data transfer velocity. The digitizer has the possibility to introduce an external trigger and an external clock.

The software used for the data-acquisition is called Wavedump [44]. It provides a user friendly acquisition interface, where events are displayed every second, and a high rate acquisition mode where events are stored in binary format. A temporal acquisition window around the incoming trigger can be set with the possibility of post and pre triggering. The window consists of \(N\) samples, where \(N\) is defined in a range from 0 to 5000. For the BaF\(_2\) crystal, only one of the two channels is needed, which makes the acquisition twice as fast. The output of the digitizer consists of a 12 bit value for each sample and a 16 bit timestamp for the trigger timestamp [45]. In this way the energy and a trigger timestamp could be evaluated for every event in the BaF\(_2\) crystal.

To be considered is the acquisition of both short and slow signals simultaneously. If pile-up shows up for the slow signal, the short signal with its higher temporal resolution could contribute for the event discrimination of multiple-hit events.

### 3.4 Synchronization

Considering the whole set-up, three parts need to be synchronized in order to measure the in- and outgoing proton track and the residual energy of the individual protons: the two TPCs and the BaF\(_2\) crystal output. To achieve this, a trigger logic unit is designed. If both SPIDR boards and the Caen digitizer are triggered with the same signal, the events could be correlated by comparing the trigger timestamps of all the units.

The logic system is given in Figure 3.15. A scintillator is placed before the first TPC as first trigger signal. The short signal of the BaF\(_2\) crystal is used as second trigger signal. The coincidence between them is taken as trigger for both the SPIDR boards and the Caen digitizer. In order not to lose any events and have a low pile-up, a logical
dead-time of 100 µs is introduced in the system. This time determines the maximum acquisition rate of 10 kHz, which is safely below the limit of 30 kHz. Furthermore, a veto on the trigger is generated when there is no acquisition, and is removed after the chips are reset. One second before the acquisition ends, the veto is inserted again.

A correlation study between the trigger timestamps of the Caen digitizer and the SPIpDR systems will confirm that the synchronization went well. Many tests at different trigger rates are performed with both random generated and controlled triggers. Figure 3.16 shows a correlation plot between the Caen digitizer and one SPIpDR board with a random trigger rate of 11 kHz. A perfect correlation between the two timestamps is observed.

![Figure 3.16](image)

**Figure 3.16** – Correlation between trigger timestamps interval of the Caen digitizer and the compact SPIpDR.

Besides the synchronization between the Caen digitizer and the SPIpDR systems, a synchronization between the two SPIpDR boards must be established. This is performed through a daisy-chain. In such a chain, one device is nominated mother board and the other slave. The trigger of the mother-SPIpDR board is propagated to the slave board and the timestamp is registered in both devices. When the acquisition starts, the mother
board starts generating the system clock and opens the shutter. Both signals are propagated, together with the trigger, to the slave board. At the end of the acquisition, the shutter is closed on both boards.

3.5 Summary and Outlook of the Set-up

A proton radiography set-up is designed, composed of two gaseous TPCs for proton tracking, a BaF$_2$ crystal for the residual energy measurement and a logic trigger system for the synchronization of the whole system. The active gas volume of the tracking detectors is $3 \times 3 \times 5$ cm$^3$. For this a gas-tight chamber had to be designed, in which an homogeneous electric field of 300 V/cm is applied. At the base of the chamber there is a triple-GEM for the electron multiplication, under which a quadboard is placed with four Timepix3 chips. The Time over Threshold, Time of Arrival and pixel position of 80 Mhits/chip/s can be recorded. A typical proton track produces $\sim 500$ hits per chip. Proton rates above the 100 kHz could then be observed using the current tracking detectors. The light collected by the PMTs, however, is digitized with a Caen digitizer at a maximum speed of 10 kHz. The limiting factor in speed is therefore the energy measurement. The resolution of the set-up will be discussed in detail in the next chapter.

A typical energy density radiograph consists of $N$ square pixels of $\sim 0.5$ mm length. Each pixel contains a number $n$ of recorded events, with a certain residual energy. It is shown by [16] that the energy distribution per pixel is Landau-distributed and thus at least 20 events per pixel are needed for a reliable fit. Considering an active area of $5 \times 3$ cm$^2$, this means that on average 120,000 well reconstructed events need to be measured. With the current proton rate of 10 kHz this would take 12 seconds. Considering the fact that a radiograph should be instantaneous ($<0.04$ sec), that the resolution should be increased ($<0.01$ mm$^2$) and that the dimensions of the radiograph should be those of a typical organ ($20 \times 20$ cm$^2$) a proton rate of $\sim 5 \cdot 10^6$ protons/cm$^2$/s is needed. The physical limitations of this set-up will then dominate: the drift-time of 5 $\mu$s and the pile-up in the BaF$_2$ crystal. Furthermore, there are technological limits due the non-zero readout times of the Timepix3 chips and the Caen digitizer. In order to overcome the limitations in the tracking detectors, multi-track events should be distinguished to increase the proton rate. For the energy measurements, the option of segmented crystals should be investigated to prevent pile-up at high proton-rates.

Studies on the increased drift region are under investigation by [46], where a TPC with a $1.5 \times 6 \times 10$ active volume is designed using a common cathode in the middle and the electron collection at the two extremities.
Chapter 4

Experiment at Proton Accelerator

Dedicated work has been performed for the building of the above described set-up in collaboration with the mechanical department at Nikhef. Special attention was paid to the construction of the TPCs. Appendix A gives a complete description on the design and construction of the TPCs. Once the functioning of the set-up was tested in the laboratory using low energetic sources such $^{90}$Sr and cosmic muons, it is brought to a proton accelerator for experiments with the proton beam.

The accelerator is called AGOR and is located at the KVI institute in Groningen. It is a cyclotron that can provide proton beams at energies up to 190 MeV at rates up to $10^{13}$ protons/s [47]. Figure 4.1 shows the set-up located in the centre of the beam. From left to right there is the scintillator, the first TPC, the phantom, the second TPC and finally the BaF$_2$ crystal. An optical alignment is performed before the experiment started. An external cooling system provides a stable temperature of the Timepix3 chips and the SPIDR readout system.

In this chapter the results of the experiment at the KVI testbeam will be discussed. For this purpose I will go through the acquisition of the detector systems, the elaboration of the acquired data to provide single proton tracks together with the TPC performance. Finally I will discuss the energy measurement and calibration and the processing of these results towards a proton radiograph.

4.1 Data Acquisition

Table 4.1 gives a summary of the settings of the TPCs during the experiment at KVI, as described in Chapter 3.

An acquisition time of 20 sec is chosen for the majority of the runs, since it is sufficiently
below the 28 allowed seconds for the SPIDR time to reset. The proton rates used range between 0.7 kHz and 4 kHz, with some test runs at the full capacity of 10 kHz.

Table 4.1 – Setting of the TPC during the experiment at KVI.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>$\text{Ar}(45%)$</th>
<th>$\text{CO}_2(15%)$</th>
<th>$\text{CF}_4(40%)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drift velocity $v_D$ [cm/µs]</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Longitudinal diffusion [µm/cm]</td>
<td>147</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transversal diffusion [µm/cm]</td>
<td>148</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active volume [mm$^3$]</td>
<td>$30 \times 30 \times 50$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric field drift volume [V/cm]</td>
<td>300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric field between GEMs [V/cm]</td>
<td>3000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric field between GEM3 and chips [V/cm]</td>
<td>5000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric field inside GEM1 [V/mm]</td>
<td>8800</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric field inside GEM2 [V/mm]</td>
<td>8600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric field inside GEM3 [V/mm]</td>
<td>8200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dead time of trigger system [µs]</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The data acquisition of the new SPIDR system in combination with the quadboard turned out to be very unstable. At more than 10% of the runs, the SPIDR was not able to detect all four the chips. Furthermore, at more than 20% of the runs, especially at high proton rates, the SPIDR readout program had a trigger timing error, due to wrongly elaboration of the external triggers. Finally, of the remaining runs only 20% resulted to have acquired an equal amount of triggers between the two detectors and the Caen digitizer. This means that only a small fraction of the acquired date will be used in the current analysis. In order to use the runs with non-equal number of triggers, offline synchronization procedures have to be applied.
4.2 Data Extraction

After the acquisition at the testbeam, the first step of the analysis is the event selection. In this section I will focus mainly on the event selection of the tracks in the TPCs. The elaboration of the energy measurements will follow in the next sections.

4.2.1 Event Selection

The extracted data of the SPIDR readout system is divided into two independent branches. The first one contains the information of the hits: Time of Arrival (ToA), fine Time of Arrival (fToA), Time over Threshold (ToT) and pixel ID. The second branch contains the time information of the trigger ($T_{\text{reference}}$). Every incoming trigger in the second branch has a set of corresponding hits in the first branch. Moreover, it is expected that there is a fixed time window between the triggertime and the ToA of the corresponding hits. The width of this so-called drift window have to be $5\,\mu\text{s}$, which is the maximum drift time of the electrons. In order to find the drift window, the time difference between a specific trigger and the ToA of all the hits is calculated. This is repeated for all the triggers. When a hit is found that corresponds to a certain trigger, the time difference will fall into the window. The hits that do not correspond to that specific trigger will be randomly distributed outside this window. Figure 4.2a shows the result of this procedure, where a peak is shown for the drift window. The time is given in units of $25\,\text{ns}$, since that is the natural unit of the Timepix3 clock. Figure 4.2b shows that the width of this window is $5\,\mu\text{s}$. Hits at the right part of this window correspond to electrons that have travelled the most and thus to electrons originating from high in the chamber. The number of hits at the right part of the drift window is almost one third of the number of hits on the left side. This is because electrons originating from high in the chamber have a higher possibility of being absorbed.

It should also be noticed that this window has a certain offset due to time delays in the software and delays in the hardware, such as finite cable lengths.

Figure 4.2 – Correlation between trigger time and Time of Arrival.
4.2.2 SPIDR Time Correction

After this event selection the data of each chip is divided into events with a certain trigger timestamp, each containing a number of hits, \( N_{\text{hits}} \). All hits have a pixel ID, a ToA, a fToA and a ToT.

From Eq. 3.1 we know that the variable \( T_{\text{Arrival}} - T_{\text{trigger}} \) is of great importance. Figure 4.3 shows a histogram on a logarithmic scale of this variable for all hits of a single run of one single chip. We would expect one single peak as shown in Figure 4.2a. However, we can observe multiple peaks with a constant time interval between them. This time interval is \( 2^{14} \) clock units, which is exactly one cycle of the SPIDR time. The reason for the multiple peak behaviour is that the SPIDR time is not always inserted correctly during the acquisition. A problem in the SPIDR software occasionally causes that a SPIDR time is missed, and the wrong SPIDR time is added to the arrival time. A correction could be applied for this SPIDR time, collecting all hits in one single peak. The result is that, already shown in Figure 4.2a and Figure 4.2b.

![Figure 4.3](image)

**Figure 4.3** – Difference between trigger time and arrival time for a single chip. A SPIDR time offset is visible between the peaks.

4.2.3 From Single Chip to Quadboard

Each TPC contains 4 Timepix3 chips. The above described procedure has to be performed for every chip. Subsequently, the hits of the 4 chips have to be combined to find the complete track over the whole chamber. This is done by comparing the trigger timestamps. If an event is found with the same timestamp of an event in another chip, the hits are combined into a single event. Figure 4.4a shows the hitmap of the quadboard which shows how the four chips are combined, while Figure 4.4b shows again the difference between the trigger time and the arrival time. The peaks are again separated. Here each peak corresponds to the drift window of the 4 chips on the quadboard. The separation between the peaks is caused by a sequential reset of the chips at the beginning of the run. By sequentially resetting the chips, the four chips will have a different
starting time. The drift window will thus be shifted for the different chips. An offline
correction can be applied in order to merge the 4 chips; however, a better solution would
be that of a simultaneous reset at the beginning of the acquisition. Unfortunately, there
was no further possibility to correct the acquisition software as this was observed after
the experiment.

Furthermore, when analysing different runs, it was found that the offset of the chips was
different for every run. An automated procedure has been developed in order to merge
the peaks by subtracting the value of the edge of the single peaks. The result of the
offline correction is that of Figure 4.5, where all the hits of the four chips are collected
inside the drift window of 5 µs.

![Figure 4.4](image)

**Figure 4.4** – Hitmap (left) and $T_{\text{Arrival}} - T_{\text{trigger}}$ (right) of the combined quadboard. An offset
if visible between the peaks of the four chips.

![Figure 4.5](image)

**Figure 4.5** – $T_{\text{Arrival}} - T_{\text{trigger}}$ after corrections for the SPIDR time and chip-offset.

After the above mentioned corrections, single tracks can be visualised. Figure 4.6a shows
the hits of a single track as function of the column number and the row number on the
quadboard. In this figure, the color indicates the value $T_{\text{Arrival}} - T_{\text{trigger}}$, which is an
indication of the height of the ionisation points. In order to obtain a three-dimensional
track, this information is translated into $x, y, z$ coordinates as shown in Figure 4.6b
In Figure 4.7 the same track is visualised, but here the color gives the ToT values of the hits. In both figures we can distinguish clear clusters. Furthermore, we observe that the ToT value in the middle of these clusters is higher than at the borders. This can be explained by reminding the triple-GEM structure. After every GEM foil, the secondary electrons will diffuse and create new avalanches in the next foil. Since the diffusion is Gaussian distributed, after three GEM foils we expect a maximum number of electrons at the location of the primary electron. The maximum of the ToT value, will then be a first approximation of the location at which the primary electron hit the first GEM foil. For a better approximation of this location, cluster finding algorithms should be used.
4.3 Track Fitting

When performing proton radiography, two parameters of the proton tracks are important: the position, which could be expressed in the centre of gravity of the track, and the angle of the proton track. In the current analysis we take $y$ as the beam direction, $x$ as the horizontal vector perpendicular to $y$, and $z$ as the vertical direction. In order to obtain the angle and the centre of gravity, a two-dimensional fit is performed in both the $xy$-plane as the $zy$-plane. Although many fitting methods are available, York’s method [48] is used in the current analysis. This method is already tested by [16] for a similar set-up with proton tracks and has proven to be a good candidate.

4.3.1 York’s Method

York’s method is an iterative method for a straight line fit. The goal is to find the solution through the data points of the function $x = a_{xy} y + b_{xy}$ for the $xy$-plane and $z = a_{zy} y + b_{zy}$ for the $zy$-plane. A set of four compact equations is obtained for the slope, the centre of mass and the corresponding errors:

$$\begin{align*}
a &= \bar{X} - b\bar{Y} \\
b &= \frac{\sum W_i \beta_i V_i}{\sum W_i \beta_i U_i} \\
\sigma_a^2 &= \frac{1}{\sum W_i} + \bar{y}^2 \sigma_b^2 \\
\sigma_b^2 &= \frac{1}{\sum W_i} \bar{u}_i^2
\end{align*}$$

(4.1)

Table 4.2 gives a summary of the meaning of the variables used in Eq. 4.1. Of great importance for this fit are the errors of the position of the hits and the weights assigned to each hit.

Hit Resolution

The uncertainties of the location of the hits are caused by finite pixel size, diffusion and timewalk. In both $x$ and $y$, the uncertainties are of equal size and given by

$$\sigma_x^2 = \sigma_y^2 = \sigma_0^2 + \sigma_{\text{diff,trans}}^2$$

(4.2)

The error $\sigma_0^2$, caused by the finite pixel size can be calculated by considering an equal hit probability on the whole pixel from $x = -1/2$ to $x = 1/2$. The standard deviation is

---

1 the equations are for the fit in the $xy$-plane, but are similarly valid for the $zy$-plane.
Table 4.2 – Summary of the notation used in Eq. 4.1

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>$X_i, Y_i$</td>
<td>Observed data points</td>
</tr>
<tr>
<td>$\omega(X_i), \omega(Y_i)$</td>
<td>Weights of $X_i$ and $Y_i$</td>
</tr>
<tr>
<td>$\alpha_i$</td>
<td>$\sqrt{\omega(X_i)\omega(Y_i)}$</td>
</tr>
<tr>
<td>$W_i$</td>
<td>$\frac{\omega(X_i)\omega(Y_i)}{\omega(X_i) + b\omega(Y_i)}$</td>
</tr>
<tr>
<td>$\bar{X}$</td>
<td>$\frac{\sum W_i X_i}{\sum W_i}$</td>
</tr>
<tr>
<td>$\bar{Y}$</td>
<td>$\frac{\sum W_i Y_i}{\sum W_i}$</td>
</tr>
<tr>
<td>$U_i$</td>
<td>$X_i - \bar{X}$</td>
</tr>
<tr>
<td>$V_i$</td>
<td>$Y_i - \bar{Y}$</td>
</tr>
<tr>
<td>$u_i$</td>
<td>$x_i - \bar{x}$</td>
</tr>
<tr>
<td>$\beta_i$</td>
<td>$W_i \left[ \frac{U_i}{\omega(Y_i)} + \frac{bV_i}{\omega(X_i)} \right]$</td>
</tr>
</tbody>
</table>

then given by:

$$\sigma^2 = \int_{-1/2}^{1/2} x^2 \, dx = 1/12, \quad \text{(4.3)}$$

yielding an error $\sigma_0$ of

$$\sigma_0 = \frac{55\mu m}{\sqrt{12}} \approx 15.9\mu m \quad \text{(4.4)}$$

The uncertainty caused by diffusion is given by

$$\sigma_{\text{diff,trans}} = D_t \sqrt{z}, \quad \text{(4.5)}$$

where $D_t$ is the diffusion coefficient given by Figure 3.4b and $z$ the drift height of the primary electrons.

Similarly, the errors in $z$ are caused by diffusion, the time resolution and additionally by timewalk:

$$\sigma_z^2 = \sigma_0^2 + \sigma_{\text{diff,long}}^2 + \sigma_{\text{timewalk}}^2, \quad \text{(4.6)}$$

where $\sigma_0^2$ is given by

$$\sigma_0 = v_{\text{drift}} \cdot \frac{25ns}{\sqrt{12}} \approx 72\mu m \quad \text{or} \quad \sigma_0 = v_{\text{drift}} \cdot \frac{1.56ns}{\sqrt{12}} \approx 4.5\mu m \quad \text{(4.7)}$$

depending on whether fToA is implement or not. The uncertainty due to timewalk is approximated as [16, 42]

$$\sigma_{\text{timewalk}} \leq v_{\text{drift}} \cdot 21ns = 21\mu m. \quad \text{(4.8)}$$
The timewalk uncertainty will not hold anymore after the timewalk correction will have taken place. On the other hand, a weight is assigned to every hit. Earlier it is discussed that the higher the ToT value, the more you approximate the ionization location. For this reason it is chosen to use the normalized ToT value as weight for the fit. The higher the ToT value, the more the hit will influence for the fit.

4.4 Detector Performance

The result of the fit is the information of the centre of gravity of each track and the slope, in both the $xy$ and $zy$ plane. In this section a study of these quantities is presented in order to analyse the performance of the TPCs. Special attention has been paid to the angular information, since one of the main goals of this research is the improvement of the angular resolution. For this analysis a run has been used, with no phantom between the two TPCs. The protons will therefore not interact significantly and the tracks observed in the two TPCs are assumed to have the same angles in the $xy$ and $zy$ plane.

4.4.1 Full Quadboard Analysis

A first analysis was done to investigate the performance of an individual TPC. This was done by using the complete track, spread over the whole quadboard of a single TPC. The angular distributions, $\alpha_{xy}$ and $\alpha_{zy}$ in the $xy$ and $zy$ plane respectively, measured in a single TPC are shown in Figure 4.8. A gaussian fit is applied to the distribution and it is found that the standard deviation of the angles is $35.9\,\text{mrad}$ and $23.8\,\text{mrad}$ for $\alpha_{xy}$ and $\alpha_{zy}$ respectively. The width of this distribution is composed of contributions from statistical fluctuations, intrinsic systematic effects of the detector and the beam divergence.

The standard deviation on the angles found with the previous set-up [16] where $18.0\,\text{mrad}$ and $52.6\,\text{mrad}$ for $\alpha_{xy}$ and $\alpha_{zy}$ respectively. The deviation in the $xy$-plane is doubled, while in the $zy$-plane it is reduced by a factor two. The larger deviation in the $xy$-plane is mainly caused by the behaviour of the triple-GEM structure, where clusters of more than 100 pixels are formed for each ionization. The typical width of such a cluster is therefore $\sim 1\,\text{mm}$. This large width causes that cluster originating from different ionizations overlap and form even larger clusters. It is especially this effect than makes it hard to distinguish the single ionizations. In the previous set-up, a GridPix detector was used [16], where only few pixels are hit for every ionization. Here the primary ionizations are easily distinguishable. On the other hand, the current TPCs are twice as long as the TPCs used in [16], where only two chips where used. This should improve the resolution with a factor $2\sqrt{2}$. Nevertheless, the clustering effects of the triple-GEM structure dominates
the resolution in the $xy$-plane.

In the $zy$-plane the clusters have a smaller spread than in the $xy$-plane, since the hits within a single cluster arrive within a small time-difference of 50 ns (which corresponds to 0.5 mm). Furthermore, in the current set-up the time of arrival is measured with an additional fast oscillator, which improves the $z$-determination with a factor 6.5. Together with the doubled TPCs and the timewalk correction that is applied using the ToT, this has halved the standard deviation in the $zy$-plane.

![Figure 4.8](image)

**Figure 4.8** – Angular distribution in the $xy$ (blue) and $zy$ (red) plane, using the full quadboard.

![Figure 4.9](image)

**Figure 4.9** – $x$ and $z$ residuals as function of $y$ after a fit using the full quadboard.

In order to find possible systematic effects, due to intrinsic properties of the TPC, the residuals of the fit are calculated. Figure 4.9 shows the residuals in the $x$-direction and the $z$-direction as function of $y$ for the two TPCs used in this experiment. Three effects are visible in both the $x$ and $z$ direction:

(i) There is an offset between the left part of the detector and the right part. In the $z$-coordinate this is due to a temporal offset between the chips. It seems that the correction
discussed in section 4.2.3 should be further improved, by adding an additional offset of 0.19 mm to the chips on the right side of the quadboard.

In the $x$-direction there is an offset due to a misalignment of the chips. The chips are glued by hand on the quadboard and can therefore deviate at the micro meter scale. The offset in the $x$-direction is negligible with respect to the other effects and will therefore not be corrected in this analysis.

(ii) If there was only an offset between the chips, a sharp offset would be expected in the residuals. However, the transition is not as sharp as expected. The reason for this behaviour at the edge of the chip is illustrated in Figure 4.11, where a cluster between two chips is show. A part of the cluster is not measured, because it fell outside the sensitive area of both chips. The position of the primary ionization is therefore moved towards the centre of the left chip. In order to correct for this effect, a cluster finding algorithm should be developed to find the most likely location of the primary electrons. The fit with only the ionization location will then be more reliable than using the whole clusters.

(iii) Moreover, at the edges of the TPC the residuals are systematically higher than in the centre of the TPC. The tracks seem to be curved at the extremities of the detector. This effect is illustrated in both the $xy$ and $zy$ planes in Figure 4.10, for $y$ greater than 24 mm. The origin of the curved tracks is an inhomogeneous electric field at the borders of the TPCs. In order to correct for this boundary effect, a cut has been applied by removing the pixels at the edges of the TPC. The results of the above mentioned corrections are summarized in Table 4.3

![Figure 4.10](image.png)  
**Figure 4.10** – 3-Dimensional track over the full quadboard in the $xy$-plane (left) and the $zy$-plane (right).
4.4.2 Single Chip Analysis

In order to better investigate the performance of the TPC, an analysis is performed by applying the fit on the hits of the individual chips. Figure 4.12 shows the chip arrangement on the quadboard. The quadboard was set at an angle of 10° with respect to the beam-direction in order to prevent the tracks to hit only single columns on the chips.

The distributions of $\alpha_{xy}$ and $\alpha_{zy}$ are shown in Figure 4.13 for the four chips individually. It is shown that the distributions of CHIP2 and CHIP3 have a non-gaussian shape in contrast to CHIP1 and CHIP4. As discussed before, the inhomogeneity of the electric
Table 4.3 – Standard deviations of the angular distributions for the full quadboard.

<table>
<thead>
<tr>
<th></th>
<th>$\sigma_{xy}$</th>
<th>$\sigma_{zy}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Quadboard</td>
<td>35.9</td>
<td>23.8</td>
</tr>
<tr>
<td>Full Quadboard (cut at edges)</td>
<td>30.7</td>
<td>27.0</td>
</tr>
<tr>
<td>Full Quadboard (cut at edges and offset correction)</td>
<td>31.0</td>
<td>23.4</td>
</tr>
</tbody>
</table>

field causes the tracks to be curved. When this inhomogeneity is not constant over the drift volume, the curvature will vary over the whole volume and the angular distributions will be non gaussian, as shown for CHIP2 and CHIP3.

In order to further investigate the behaviour of the single chips, the residuals are again calculated. The result is shown in Figure 4.14. Although the residuals for the single chips are significantly smaller, they show a parabolic effect in the $xy$-plane for CHIP1.
and CHIP4. This effect indicates that the tracks are curved at both ends. CHIP2 and CHIP3 on the other hand, seem not to be affected; however, the angular distributions show a non-gaussian behaviour.

![Figure 4.14 – Residuals of the fit on the four chips independently.](image)

For a better understanding of this behaviour, the mean of the angular distribution is calculated as function of $x$ and shown in Figure 4.15. The mean of the angular distribution is linearly dependent on $x$ for CHIP2 and CHIP3, while in CHIP1 and CHIP4 it is almost constant. As shown in Figure 4.14 the residuals show a symmetric parabolic effect for CHIP1 and CHIP4. This effect is caused by the fact that the tracks are curved at both ends in the same direction which will cause a shift in position, but no significant change in the reconstructed angle. CHIP2 and CHIP3 on the other hand, show no systematic effect in the residuals, but the curvature strongly depends on the $x$-location of the track and therefore affects the angular distributions as shown in Figure 4.14.

This difference may be caused by the location of the different chips on the rotated quadboard (see Figure 4.12). The right edge of CHIP2 will be more affected by the inhomogeneous electric field than the left part since it is located closer to the edge of the drift chamber. On the other hand, tracks that pass through CHIP1 are more likely to be curved at both extremeties since the location of this chip causes a more symmetric behaviour of the inhomogeneous electric field.
Unfortunately, in the time frame of this thesis no correction can be applied for the inhomogeneous behaviour of the electric field. In future studies particular attention should be paid to this effect. A similar study, where a GEM based TPCs was used, showed comparable problems with the electric field [46]. It was pointed out that the homogeneity of the electric field is particularly sensitive to the tuning of the last strip on the drift cage.

For the remaining part of the analysis, only the tracks that pass through the central part of the detector are used, since the mean angle of the four chips have a major overlap in that region and the effect of the inhomogeneous electric field is minimized. The calculated deviations for this region are summarized in Table 4.4.

**Table 4.4** – Standard deviations of the angular distributions of tracks going through the central region of the quadboard calculated for the single chips.

<table>
<thead>
<tr>
<th></th>
<th>$\sigma_{xy}$</th>
<th>$\sigma_{zy}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHIP1</td>
<td>41.1</td>
<td>32.8</td>
</tr>
<tr>
<td>CHIP2</td>
<td>36.3.8</td>
<td>35.4</td>
</tr>
<tr>
<td>CHIP3</td>
<td>33.1</td>
<td>31.7</td>
</tr>
<tr>
<td>CHIP4</td>
<td>39.7</td>
<td>33.4</td>
</tr>
</tbody>
</table>
For a better estimation of the angular uncertainties of the single chips, a correlation study is performed between the angles of the chips. A track that passes CHIP1 and CHIP2 is expected to have the same angle in the two chips, which leads to a high correlation factor. If however, the distributions are dominated by the uncertainties, the correlation will vanish. Figure 4.16 shows the results of this study, where $\alpha_{xy,CHIP1}$ is plotted against $\alpha_{xy,CHIP2}$ (left), and $\alpha_{zy,CHIP1}$ is plotted against $\alpha_{zy,CHIP2}$ (right). For the angles in the $xy$-plane a correlation factor of 0.43 is found, while the correlation factor in the $zy$-plane is found to be only 0.006. It could be concluded that in the $zy$-plane the angles are dominated by the angular uncertainties, and are thus uncorrelated. In the $xy$-plane the beam divergence seems to dominate over the angular uncertainties and therefore the angles are more correlated. It could be concluded that the beam-divergence in the $xy$-plane is larger than in the $zy$-plane. Further studies on the beam characteristics should be done in order to better understand this effects.

Finally, the information of the single chips can be recombined to obtain a better angular resolution. Two methods are discussed here. The first method is by averaging the angles of CHIP1 and CHIP2. The resulting angular distribution is shown in Figure 4.17. The standard deviations are 47.1 mrad and 25.1 mrad for the $xy$-plane and the $zy$-plane respectively. A slight improvement is obtained in the $zy$-plane, while the results of the $xy$-plane remain unchanged.

The second method involves the centre of gravities of the track, calculated for the single chips. The angles between the centre of gravities on the different chips are used to determine the direction of the protons. Figure 4.18a, shows the position difference between the centre of gravity in CHIP1 and CHIP2, both in $x$ and $z$. The deviations are calculated to be 0.53 mm and 0.38 mm for $x$ and $z$ respectively over 15 mm in $y$. This large spread already indicates that the angular resolution will not be higher than
27 mrad. Figure 4.18b shows the angular distribution using the centre of gravities. The standard deviations are calculated to be 43.6 mrad and 36.8 mrad in the $xy$-plane and the $zy$-plane respectively. This bad resolution is mainly caused by the high position uncertainties discussed before.

It can be concluded that the best angular resolution is obtained by performing the fit over the full quadboard, after the correction for the temporal offset between the chips and a
cut on the edges of the TPC. Due to the dominant effects of the triple-GEM structure the angular resolution in the $xy$-plane is decreased by a factor two with respect to the previous set-up, even with a factor $2\sqrt{2}$ improvement included. In the $zy$-plane the resolution is increased by a factor two due to the increased size of the TPC and the increased temporal resolution. However, the expected scattering angles between 5 mrad and 20 mrad are still far below the detector resolution.

4.5 Energy Measurement

Finally, for the proton energy-loss radiograph the residual energy measurement is performed with the BaF$_2$ crystal in combination with the Caen readout system. The peak voltage of every event is translated into a specific energy through a calibration. The AGOR facility has the possibility to insert degraders of various thickness into the beam. Depending on the thickness, the protons will have a given energy between 0 and 150 MeV. Figure 4.19 shows the histograms of the peak voltages for different energies. A gaussian fit is performed for every energy in order to obtain a relation between the peak voltage and the energy. In Figure 4.19 the effect of the degraders is visible. The histograms corresponding to the lower energies and thus thicker degraders are wider than the histograms corresponding to the higher energies.

![Histogram of peak voltages for different energies at the same beam intensity.](image)

A second effect was found when comparing the peak voltages of the same energy calibrations but at different proton rates. At high proton rates, the PMT has less time to restabilize than at low proton rates. The output voltage will therefore be lower for high proton rates. This effect is shown in Figure 4.20 for two calibrations at 1 kHz and 5 kHz.
with a proton energy of 100 MeV. To obtain the full calibration, first a linear beam rate correction needs to be performed of the form:

\[ V_{\text{cor}} = V_{\text{peak}} \cdot (0.93 + 9 \cdot 10^5 \cdot \text{beam intensity}) \]  

(4.9)

It was discussed in Section 3.3.2 that the short signal of BaF_2 crystal could be used for a higher beam intensity. It should be investigated if this signal shows a similar rate dependency and what the effect is on the energy calibration. At same intensities it is expected that the PMT has more time to recover, due to the short duration of this signal; but the behaviour at higher intensities should be further investigated.

After the correction for the beam intensity, the energy calibration can be performed. Figure 4.21 shows the different energies as function of the corrected peak voltage. The result is a third order polynomial fit through the data points and is given in table 4.5.

**Table 4.5** – Fit results of the energy calibration, where the function \( E = p_0 + p_1 V_{\text{cor}} + p_2 V_{\text{cor}}^2 + p_3 V_{\text{cor}}^3 \) was used.

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>( p_0 )</td>
<td>( p_1 )</td>
<td>( p_2 )</td>
<td>( p_3 )</td>
</tr>
<tr>
<td>43 ± 12</td>
<td>( 6.1 ± 3.5 ) ( \times 10^{-2} )</td>
<td>( -5.8±3.3) ( \times 10^{-3} )</td>
<td>( 3.4±1.0) ( \times 10^{-8} )</td>
</tr>
</tbody>
</table>
4.6 Phantom Reconstruction

During the experiment at KVI the phantom shown in Figure 4.22 was used. Only the part within the $5 \times 3 \text{ cm}^2$ red box was imaged, since that is the maximum active area of the two TPCs. In order to reconstruct this phantom, the entry and exit location of the protons on the phantom are calculated extrapolating the position in the detectors on the phantom. With the additional information of the deposited energy, an energy-loss radiograph can be constructed. It was already discussed that with the obtained angular resolution no scattering radiograph can be reconstructed.

![Figure 4.21](image_url) – Different energy measurements as function of the corrected peak voltage.

![Figure 4.22](image_url) – Picture of the phantom used at the experiment at KVI.
A good approximation for the reconstruction of an energy-loss diagram is to use only the TPC before the phantom, calculate the entry location of the protons and relate it to the measured energy deposition. The plane on the phantom is divided in bins of 0.5 mm$^2$, where each bin contains the mean energy of all the tracks that entered the phantom at that location. Figure 4.23a shows the result of this radiograph obtained with an exposure time of 10 seconds at a beam intensity of $\sim 2$ kHz for a total of 22,000 reconstructed proton tracks. A very bad contrast is obtained due to the low angular resolution.

A better resolution is obtained by assuming that the protons before the phantom are travelling in a straight line. With this assumption, the centre of gravities only can be used to calculate the entry location on the phantom. The result of this procedure is shown in Figure 4.23b using the same number of reconstructed protons. The cylinders of Figure 4.22 are distinguishable in blue. The green region corresponds to the PMMA of the phantom, where the energy loss is higher than in the cylinders that are different types of tissue. Furthermore, at the top and the bottom of the radiograph there are regions with a high energy loss. This high energy loss is caused by the intersection of the protons with the GEM stack and the cathode.

Figure 4.23 – Energy-loss radiograph using the angles or only the centre of gravity of the proton track.

Figure 4.24 shows the same results as in Figure 4.23b, but with an exposure time of 100 seconds at a beam intensity of 3 kHz for an image with high statistics. Table 4.6 gives a summary of the measured energy loss of the different regions of the phantom and the theoretical predictions for the given materials. The expected energy loss in 6 cm PMME is 37.8 MeV, where the measured energy loss is 40 MeV. The upper-left half-cylinder corresponds to liver. The expected energy loss is 31.5 MeV, while the observed energy
loss is 35 MeV. The lower cylinder is made of breast, where the expected energy loss is 28.3 MeV and the measured value is 30 MeV. Finally, the largest cylinder corresponds to a mixture of fat, air and solid water. Here the predicted energy loss is 16.8 MeV and the measured value is 20 MeV.

If we compare the measured values with the prediction, we find systematically that the measured value is higher than the expected value. As we know that the output of the calorimeter depends on the beam intensity, it is possible that this discrepancy is caused by the energy calibration. In future experiments the behaviour of the calorimeter at different beam intensities should be further investigated for a correct energy calibration. Furthermore it is important to maintain a constant beam intensity during the whole experiment. In the experiment performed at KVI the beam intensity oscillated between 0.7 kHz and 4 kHz, with few exceptions of 10 kHz test runs.
Table 4.6 – Measured an expected energy losses in the phantom.

<table>
<thead>
<tr>
<th>Material</th>
<th>Theory (MeV)</th>
<th>Experiment (MeV)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMMA</td>
<td>37.8</td>
<td>40</td>
<td>6%</td>
</tr>
<tr>
<td>Liver</td>
<td>31.5</td>
<td>35</td>
<td>11%</td>
</tr>
<tr>
<td>Breast</td>
<td>28.3</td>
<td>30</td>
<td>6%</td>
</tr>
<tr>
<td>Fat, air, solid water</td>
<td>16.8</td>
<td>20</td>
<td>19%</td>
</tr>
</tbody>
</table>
Chapter 5

Conclusions and Outlook

With the increased number of proton therapy centers there is a renewed interest in proton radiography. In this study a set-up is built to measure the position, direction and energy of protons that traverse an object in order to reconstruct an image of that object. The set-up consists of two GEM-based TPCs with a Timepix3 quadboard as basis and a BaF$_2$ crystal for the energy measurement.

The Timepix3 quadboard in combination with the SPIDR readout was tested successfully. Nevertheless, the readout software should be improved for the temporal offset between the chips and for the bad allocation of the SPIDR time.

Although the sensitive area of the TPC is doubled and the improved temporal resolution of the Timepix3 is included, the angular resolution is still insufficient to use the angular information for the phantom reconstruction. These uncertainties are dominated by the clustering effect of the triple-GEM structure and the inhomogeneity of the electric field inside the TPC. Cuts where applied at the edges of the TPC, where the electric field was more distorted. In order to better control the clustering effect, an algorithm should be developed in order to find the location of the primary ionization. The most likely location of the primary ionization is the position of the maximum ToT in each cluster. The track fit using only the location of the primary ionization will be more realistic than using all the hits of the clusters.

The final angular resolution obtained with the current set-up is $30.7\, \text{mrad}$ in the $xy$-plane and $23.4\, \text{mrad}$ in the $zy$-plane.

Furthermore, studies have been performed in order to increase the beam intensity that the set-up can handle. Due to its data-driven and zero-suppressed readout, the Timepix3 chip is able to measure 80 Mhits/s. The average number of hits of a single proton track using a GEM-based TPC is 800 hits/chip. The current TPCs is thus able to observe 100 000 tracks/s. In previous studies, where GridPix based TPCs were used, it was
shown than the number of hits of a single proton track was only 100 hits/chip. The use of GridPix in stead of GEM foils has thus the advantage of a low number of hits for a faster readout up to 800 000 tracks/sec. Moreover, single electrons are easily visible using a GridPix based detector, while the clustering effect of the triple-GEM structure needs a cluster-finding algorithm to obtain the ionization location.

The readout of the calorimeter is improved from 50 Hz to 10 kHz due to the implementation of the Caen readout system. This limit could be further increased by a factor ten using only the short signal of the BaF$_2$ crystal and using an optical link connection instead of the usb-interface. It should be investigated if the short pulse has a similar intensity dependency as was found for the slow pulse. Due to its short duration it is expected that the PMT has sufficient time to restabilize before a second pulse is recorded and will therefore be less sensitive to the intensity. Moreover, the possibility of a segmented crystal should be investigated to further increase the beam intensity.

With the current intensity of 10 kHz, in 12 seconds, sufficient protons can be observed in order to reconstruct a phantom with a surface of $5 \times 3 \text{ cm}^2$.

Figure 4.24 shows the energy-loss radiograph of a phantom, obtained at KVI. Here only the centre of gravity is used to determine the entry location on the phantom. The total exposure time was 100 seconds at a beam intensity of 3 kHz for a high statistics image.

Further improvements on the determination of the entry angle can be obtained by installing two TPCs before the phantom. If the distance between the two detectors is large, the centre of gravity of the track in the two detectors can be used to determine the angle with great precision. The disadvantage of two detectors before the phantom is that the protons will scatter more due to the second TPC.

In order to improve the angular resolution after the phantom, a silicon based telescope can be used. These detectors are known for their high resolution, but also for the high beam interference. Such a device should be avoided before the phantom because the protons will scatter on the detector itself and therefore affect the image resolution. After the phantom, the scattering with the detector is of less importance because the proton already scattered through the whole phantom. The silicon telescope could thus be used here in place of the TPC.

In addition to the improvements on the beam intensity and the angular resolution, also the total active area should be increased. For clinical purposes a $5 \times 3 \text{ cm}^2$ area is not enough. A complementary study is performed at Nikhef with a similar set-up, based on the Timepix chip, to increase the active area [46]. The goal of this study was to achieve an active area of $6 \times 10 \text{ cm}^2$; however, due to technical problems during the experiment.
at KVI there was no possibility of reconstructing a phantom with this set-up.

Once the above mentioned problems are solved and an angular resolution below 1 mrad is reached, a step towards proton-CT can be done by irradiating the phantom from different angles. A 3-dimensional energy density map can then be reconstructed to improve future proton therapy treatment plans.
Acknowledgment

During these years as physics student I met a lot of persons who helped me with my studies and with which I had a great time. I would like to put some acknowledgements here, knowing that I will certainly forget someone.

First of all I would like to thank my supervisor, Jan, for the opportunity he gave me to work in his team, but also for all the "pizzate" at his place and for his advices in all fields.

To Els for her advice, specially in the last period of my research, for the careful reading of my thesis and for the many discussions of the results of my experiment.

To Martin that was always there with his experience in everything and to Bas, Nigel and John that helped me a lot with all the programming and electronics.

To all the people that gave me technical support at nikhef but also at Cern: Oscar, Berend, Ad, Wim and Fabrizio.

To my colleagues here at Nikhef for the beautiful times we had during this year: Nathalie, Duco, Froukje, the two Kevins, Tom, Michele, Stergios, Panou, Enrico, Francesco, Rolf, Priscilla, Ivan and all other phd students at Nikhef.

To all other physics student with which I had a great time during all my courses and specially during the breaks where we had numerous nintendo and ping-pong matches: Mick, Tim, Judith, Ruud and many other..

Per la mia numerosa famiglia: i miei genitori (che sono ancora convinto non abbiamo mai capito niente di quel che faccio), fratelli, sorelle, cognati e nipoti (specialmente Samu).

A particular "thank you" goes to a great friend that was always there for me: Daniele.

Alla mia "futura mogliettina", Caterina. Anche se questi anni siamo stati stati sempre molto lontani, sei stata il mio più grande aiuto a finire anche questo periodo della mia vita.

L’unico problema che resta da risolvere è la minimizzazione dell’integrale sul tempo del modulo della differenza dei nostri vettori posizione. Ti ho sempre promesso che avrei inventato la macchina per il teletrasporto per risolvere questo problema, ma penso che ben presto non ce ne sarà più bisogno! 😊

Finally I would like to thank God for the beautiful creation that we physicist have the honour to think to understand.

Paolo Radaelli
Amsterdam, 2015
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