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A Pixel Detector Characterization for the Quality Assurance

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The important thing is not to stop questioning. Curiosity has its own reason for existing. One cannot help but be in awe when one contemplates the mysteries of eternity, of life, of the marvellous structure of reality. It is enough if one tries to comprehend only a little of this mystery every day.

Albert Einstein

Abstract

Proton therapy using Pencil Beam Scanning (PBS) offers highly conformal dose distributions for cancer treatment, maximizing tumor control while minimizing damage to surrounding healthy tissues. However, the extreme precision of PBS demands rigorous and efficient Quality Assurance (QA) protocols to guarantee patient safety. QA systems require very high spatial resolution ($\sigma_{x,y} < 1-2\text{ mm}$) to verify complex, heavily modulated dose fields and must be as time-efficient as possible.

This thesis focuses on the characterization and dose calibration of a novel high-resolution pixel detector system designed for advanced QA applications. The work was carried out at the Center for Proton Therapy (CPT) at the Paul Scherrer Institute (PSI). Measurements were performed at the Gantry 2 treatment room, comparing the pixel detector's response with standard dosimetric devices and Monte Carlo simulations implemented in TOPAS. The core objective of the project was to derive and validate a reliable dose conversion factor to translate the raw signal collected by the pixel detector into absolute dose values. This work successfully demonstrated the capabilities of the device, particularly its excellent 2D spatial resolution of delivered spots. However, the full characterization of the detector is not yet complete. During the analysis, deviations from reference values were observed, and a specific structural limitation of the device was identified. Since this was not found to be the sole source of error, these factors must be carefully considered to perform correct quality assurance measurements. Ultimately, this work outlines the current limitations of the detector and highlights the need for further studies and future tests to complete its full validation.

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Introduction

Cancer remains one of the most complex and challenging diseases to treat, representing a leading cause of mortality worldwide. In 2022, there were nearly 20 million new cancer cases. That same year recorded 9.8 million deaths, corresponding to a mortality-to-incidence ratio of nearly 50% [1]. Within the multidisciplinary approach to oncology, radiotherapy plays a fundamental role in tumor control. Over the past decades, technological advancements have continuously aimed at a single, critical objective: maximizing the lethal radiation dose delivered to the tumor while sparing the surrounding healthy tissues and critical organs at risk.

In this context, proton therapy has emerged as a superior modality for specific clinical indications. Unlike conventional X-ray radiotherapy, which deposits energy exponentially along the beam path, protons deposit the majority of their energy at a very specific depth, known as the Bragg peak. This physical advantage has been fully exploited with the advent of Pencil Beam Scanning (PBS), a technique pioneered at the Paul Scherrer Institute (PSI). By dynamically sweeping a narrow proton beam in three dimensions, PBS allows for the "painting" of highly conformal dose distributions tailored precisely to the complex shapes of individual tumors.

However, the extreme precision of PBS demands highly precise delivery control. Because the dose is delivered through thousands of highly localized, high-gradient beam spots, any slight deviation in beam position, energy, or intensity can lead to severe dosimetric errors. To guarantee patient safety and treatment efficacy, rigorous Quality Assurance (QA) procedures are mandatory. Routine QA verifications need to be as time-efficient as possible and require very high spatial resolution to capture the steep dose gradients of modern Intensity-Modulated Proton Therapy (IMPT) plans. Consequently, there is a strong clinical need for innovative, fast, and high-resolution 2D detector systems capable of streamlining the QA workflow.

This thesis addresses this need by investigating a novel pixel detector system for QA purposes. The research was conducted during an internship at the Center for Proton Therapy (CPT) at PSI. The primary objective of this project is to characterize and calibrate the pixel detector to perform validated absolute dose measurements. While previous studies have confirmed the uniformity of the gain response across the detector's pixels, this work focuses specifically on the *dose calibration*: deriving a robust conversion scaling factor to accurately calculate the delivered dose from the raw signal collected by the device.

The structure of this thesis reflects the progression of the project, from theoretical foundations to experimental validation:

- **Chapter 1** introduces the fundamental physics and clinical principles of particle and proton therapy, explaining the physical interactions of protons with matter and the rationale behind modern radiotherapy techniques.

- **Chapter 2** provides an overview of the CPT facility at the Paul Scherrer Institute. In particular, the PROSCAN project and the Gantry 2 treatment room are described, as this is where all the data acquisition campaigns for this project were performed.
- **Chapter 3** describes the hardware and architecture of the pixel detector. The working principles, readout electronics, and current limitations of the system are presented.
- **Chapter 4** focuses on the data acquisition process. The experimental procedures used to obtain data with the pixel detector and the main delivered dose fields are illustrated. Additionally, the data-taking process with standard reference devices and the implementation of setup and beam simulations using TOPAS are detailed.
- **Chapter 5** explores the data analysis procedures and results obtained. The dosimetric performance of the pixel detector is evaluated, and the formal dose calibration procedure to obtain the absolute scaling factor is illustrated. Finally, the tests performed to validate the calibration process against standard QA measurements are discussed.

1 Treating Cancer with Protons

In this chapter, the focus will be on how to use particles, in particular protons, to fight cancer. At the beginning, an overview of particle therapy is given. Then, the attention is shifted toward proton therapy. The physical description of protons interaction with matter, the main techniques used in clinics and the different approaches to build a proton facility are explored. At the end, the impact of proton therapy around the globe is illustrated.

1.1 General Introduction on Particle Therapy

Radiotherapy is a clinical technique primarily employed for the treatment of tumors, aiming to eradicate cancer cells while minimizing damage to surrounding healthy tissues. This is achieved by delivering ionizing radiation to the target volume.

Radiation therapy is an important component of cancer treatment with approximately 50% of all cancer patients receiving radiation therapy during their course of illness; it contributes towards 40% of curative treatment for cancer [2].

1.1.1 Mechanisms of Cell Damage

The biological effect of radiation is essentially based on its ability to damage the DNA of cells, inhibiting their replication and eventually leading to cell death. At the baseline of this cellular death mechanism is the *p53* gene, which interrupts cellular growth and division if DNA damage, that the cell is unable to repair, is detected [3].

DNA can be damaged through two distinct mechanisms: direct and indirect.

The first mechanism consists of the direct absorption of radiation by the DNA molecule, which ionizes certain bonds, thereby removing one or more nitrogenous bases (see Figure 1). In the event that a single nitrogenous base is removed—a phenomenon known as a *Single Strand Break* (SSB)—the damaged information can be easily recovered thanks to the complementary strand in approximately 99% of cases. Conversely, if complementary pairs of nitrogenous bases are successfully removed, it results in a *Double Strand Break* (DSB). This type of damage proves significantly more difficult to repair, with successful restoration occurring in only about 88% of cases.

Another type of damage can occur indirectly through the radiolysis of water, which constitutes the majority of the cellular volume. In this process, the radiation ionizes a water molecule inside the cell, and the ejected free electron subsequently ionizes another water molecule negatively:





Figure 1: *Schematic representation of a Single Strand Break (left) and a Double Strand Break (right) induced on the DNA structure.*

Following this primary ionization, the two unstable ions H_2O^+ and H_2O^- dissociate to generate the free radicals H° and OH° , accompanied by a hydrogen ion H^+ and a hydroxide ion OH^- :



These newly formed radical molecules are highly reactive and can readily interact to produce hydrogen peroxide (H_2O_2), which is highly toxic to the cell environment and ultimately leads to cell death.

1.1.2 Dosimetric Quantities, LET, and RBE

To fully understand the radiobiological effects of different types of radiation, it is necessary to introduce the physical "dosimetric" quantities that describe energy transfers, alongside the Linear Energy Transfer (LET) and the Relative Biological Effectiveness (RBE) [4].

The primary dosimetric quantity is the *absorbed dose* (D), defined as the energy absorbed per unit of mass:

$$D = \frac{dE}{dm} \quad (5)$$

It is measured in Gray (Gy), which corresponds to J/kg. However, the absorbed dose does not take into account the biological effects caused by different types of radiation or different energies. For this reason, a new quantity called *equivalent dose* (D_{eq}) is introduced. This is the absorbed dose weighted by a factor related to the radiation quality R (reflecting the specific hazard of different types of radiation on biological tissues),

known as the radiation weighting factor, denoted by w_R , summed over all different types of radiation:

$$D_{eq} = \sum_R w_R \cdot D_R \quad (6)$$

Furthermore, since different organs and tissues possess varying radiosensitivities, it is convenient to define the *effective dose* (D_{ef}). This is the sum of the equivalent doses across all tissues and organs T of the body, each weighted by a specific tissue weighting factor w_T :

$$D_{ef} = \sum_T w_T \cdot D_{eq,T} \quad (7)$$

Both equivalent and effective doses are measured in Sievert (Sv), which represents the dose in Gray multiplied by these quality factors.

Because the non-specificity of the absorbed dose creates limitations when discussing biological damage, it is essential to consider the *Linear Energy Transfer (LET)*. The LET defines the energy transferred by a primary ionizing particle to the traversed material per unit of path length ($LET = dE/dx$). As illustrated in Figure 2, high-LET radiations (such as heavy ions or low-energy protons) deposit a large amount of energy over a short distance, causing dense and clustered ionizations that are more likely to induce complex, unrepairable DNA double-strand breaks. Conversely, low-LET radiations tend to produce more sparse, isolated damage.

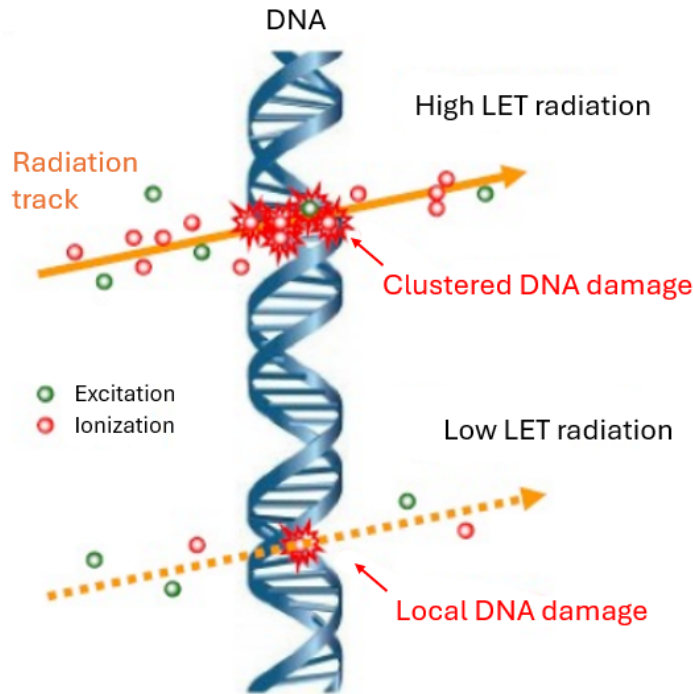


Figure 2: *Type of damage caused by high or low LET beams.*

Finally, to account for the different biological effects at varying LETs, the National Bureau of Standards introduced the *Relative Biological Effectiveness (RBE)*. It is defined as the

ratio of a dose of a reference radiation (D_X) required to produce a certain biological effect to the dose of the test radiation (D_R) that produces the same effect:

$$RBE = \frac{D_X}{D_R} \quad (8)$$

1.2 Proton Therapy

1.2.1 Historical Background

The existence of protons was first demonstrated by E. Rutherford in 1919 [5]. However, the therapeutic potential of the depth-dose characteristics of protons was first recognized in a seminal report by R. R. Wilson in 1946 [6]. Wilson theorized that it would be easy to produce well-collimated narrow beams of fast protons, and due to the fact that the range of the beam is easily controllable, the precise irradiation of small volumes inside the body would become a reality. He also described the use of a rotating wheel of variable thickness—a range modulation wheel (RMW)—interposed in a proton beam as a method to superimpose several Bragg peaks of variable energies to create a uniform dose region.

The first patients were treated with proton beams in 1955 at the Lawrence Berkeley Laboratory in California. Until about 1990, a number of research accelerators at physics laboratories around the world were adapted for treating cancer patients. These laboratory-based facilities had numerous limitations, including restricted beam orientations (typically horizontal beams only), competition for beam-on time, and inadequate medical logistics. The modern clinical era of particle therapy began in 1990 when the first hospital-based proton therapy facility was established at the Loma Linda University Medical Center in California [7, 8] using a Fermilab-designed 250 MeV synchrotron. The Loma Linda facility pioneered the delivery of a single source beam to more than one treatment room, enabling multiple patient treatments, although not simultaneously due to the time required to switch from one room to another. Loma Linda also demonstrated the clinical use of rotating gantry systems (see Section 1.2.5) that deliver protons into a patient from a number of directions, which avoids the need to rotate the patient other than in the horizontal plane, whilst essentially still providing treatment beams from any angle.

Important discoveries helped in the development of proton therapy: the introduction of CT imaging enabled model-based treatment planning and accurate Bragg peak placement. Moreover, the development of pencil beam scanning (PBS) as an innovative delivery technique (see Section 1.2.3), pioneered by Pedroni at Paul Scherrer Institute (PSI), enabled Intensity Modulated Proton Therapy (IMPT) and fundamentally transforming dose-shaping. Today, PBS is the dominant clinical technique worldwide.

1.2.2 Conventional Radiotherapy vs. Proton Therapy

There is a substantial difference between the use of conventional radiation (photons) and hadronic particles (such as protons) for therapeutic purposes, which mainly arises from how these particles interact with matter and deposit their dose in the tissues [9].

Conventional radiotherapy typically utilizes high-energy X-rays (photons). The interaction of photon radiation with matter occurs primarily through three distinct processes [10]:

- Photoelectric effect
- Compton scattering
- Pair production

As a result of these interactions, a photon beam does not have a well-defined range. Instead, it exhibits an exponentially decreasing depth-dose profile. The maximum dose is deposited at a relatively shallow depth (near the entrance skin) and continues to deposit significant energy beyond the target volume, inevitably exposing the healthy tissue located behind the tumor to unwanted radiation (see Figure 3).

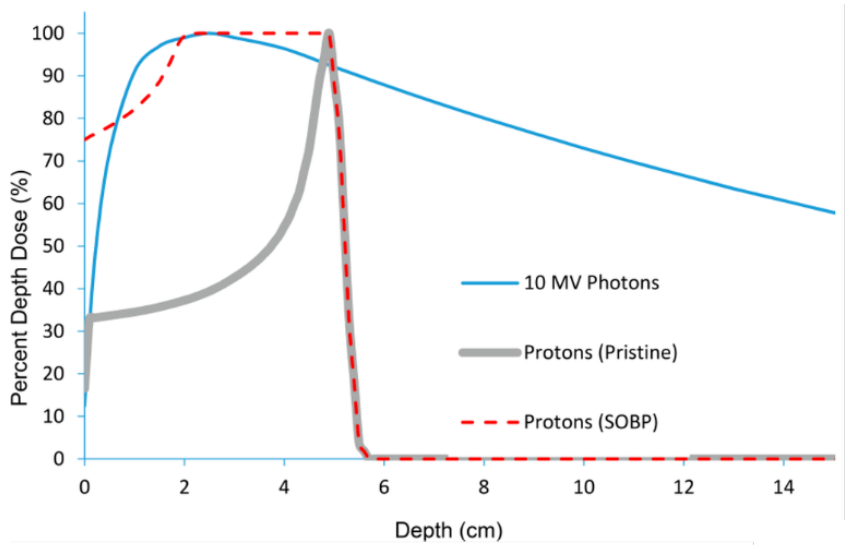


Figure 3: Plot showing the different depth-dose curves between protons and photons.

The primary advantage of proton therapy lies in the unique physical properties of heavy charged particles. Unlike photons, protons lose energy as they traverse matter predominantly through inelastic Coulomb scattering with atomic electrons. The mean rate of this energy loss is described by the *Bethe-Bloch formula* [10]:

$$-\frac{dE}{dx} \propto \frac{z^2}{v^2} \ln \left(\frac{2m_e v^2}{I} \right) \quad (9)$$

where v is the velocity of the incident particle, z is its charge, m_e is the electron mass, and I is the mean excitation potential of the target material.

Because the energy loss is inversely proportional to the square of the particle's velocity ($1/v^2$), protons deposit a relatively low and constant dose at the entrance of the tissue when they are traveling fast. However, as they slow down, their energy loss rate drastically increases. This leads to a massive localized release of energy just before the particle comes to a complete stop.

This localized maximum of energy deposition is known as the *Bragg Peak* [10]. Immediately beyond the Bragg peak, the dose abruptly drops to zero. The depth of the Bragg peak is modulated by the initial energy of the beam. While highly localized, a pristine peak is not infinitely sharp; its longitudinal width is primarily dictated by *range straggling*, which arises from the statistical fluctuations in the energy loss process as protons travel through matter. Because these fluctuations accumulate along the particle's path, the straggling effect, and consequently the width of the Bragg peak, increases with the initial energy of the beam. In typical clinical scenarios, the width of a single pristine peak varies from approximately 2 mm at low therapeutic energies to about 8-10 mm at the highest energies.

However, it often happens that the tumor volume to be irradiated has a longitudinal size significantly greater than the width of a single pristine peak. In this case, it is necessary to use multiple beams at different energies. This technique leads to the *Spread Out Bragg Peak (SOBP)*, which is the uniform dose plateau relative to the total dose curve given by the superposition of the effects of each individual beam (see Figure 4). Instead, to cover the cancer volume laterally, two main techniques are implemented and are described in the next section (1.2.3).

1.2.3 Beam Delivery Techniques

The initially narrow beams of protons entering the treatment nozzle, which is the final output assembly of a radiation therapy machine, must be spread laterally and longitudinally to conform to the 3D shape of the tumor. The evolution of these delivery techniques dictates the hardware requirements of the entire facility [11, 12].

Passively Scattered Proton Therapy (PSPT)

Historically, Passively Scattered Proton Therapy (PSPT) was the standard delivery method. Passive scattering (see fig. 5) typically uses two scattering layers, in which the first (primary) scatterer spreads the beam out laterally and a second, about half the distance between first scatterer and patient, has a complex variation of thickness with distance from beam axis to provide a dose that is uniform in intensity across the treatment field width [11]. With a double-scattering design, lateral conformation to the tumour can be achieved using either multi-leaf collimation (MLC), analogous to that used in x-ray radiotherapy systems, or by manufacturing a custom collimator for each individual patient

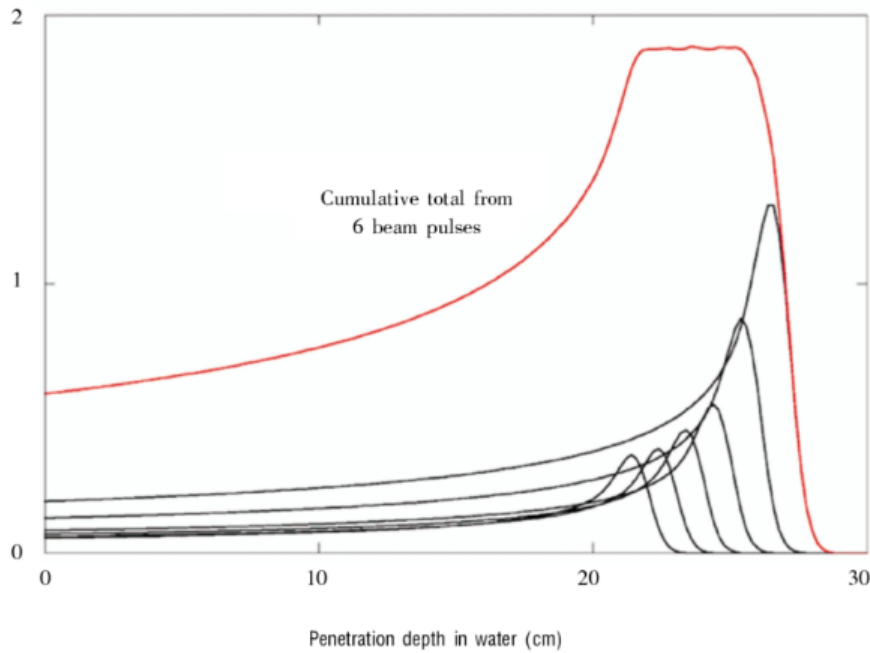


Figure 4: *The superposition of proton beams of different energies (black lines) results in the formation of the SOBP (red line), which provides a uniform dose over the entire target region.*

treatment. However, the use of such collimation in the treatment nozzle can produce an additional neutron dose for the patient. It is also possible to avoid scattering using a set of so-called wobbler magnets that paint the beam in a series of concentric circles, along with collimators to establish the lateral field shape.

Longitudinal conformation is achieved using the well-established technique of utilising a range modulator and compensator, the latter being manufactured specifically for each patient treatment. These are typically manufactured from a polymer, the modulator being a spinning, wedged wheel (usually called Rotating Modulation Wheel or RMW), generating a SOBP covering the tumour longitudinally; an example is shown in Figure 6.

The compensator is a fixed-energy degrader conformed in thickness laterally across the tumour to have the distal edge of the SOBP follow the distal edge of the tumour. This arrangement does not provide optimal conformation to more complex target volumes, since the constant depth range delivered may be larger than the tumour in some locations, resulting in a "pull-back" of high-dose delivered in more superficial healthy tissues [8]. To achieve three-dimensional conformation, a range-stacking procedure must be used; the treatment volume is divided into a series of depth slices, each with a given outline determined by the MLC settings. By treating each depth slice sequentially, an irregular treatment volume can be covered with higher precision.

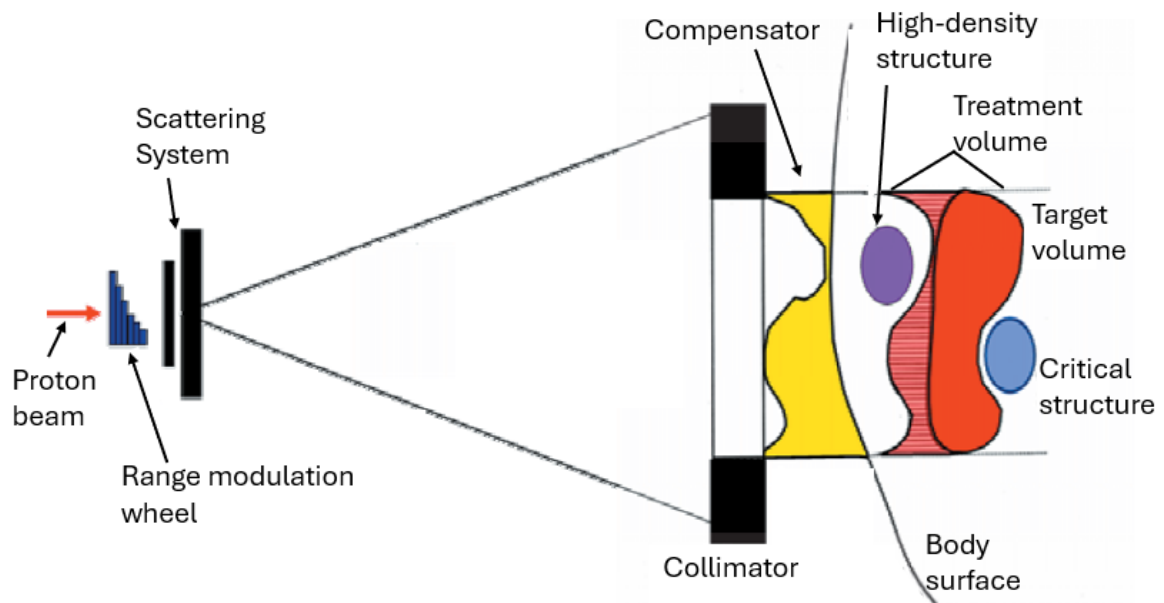


Figure 5: *Scheme of passively scattered proton therapy technique from [8]*

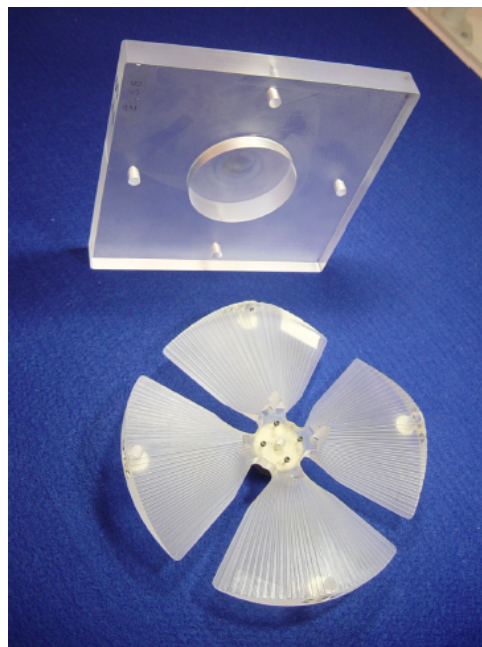


Figure 6: *Compensator (top) and range modulator (bottom) used at Clatterbridge Hospital from [11]*

Pencil Beam Scanning (PBS) and IMPT

A more efficient and clinically advanced alternative is magnetic spot scanning, or Pencil Beam Scanning (PBS) (see Figure 7). In this approach, sets of orthogonal scanning magnets deflect the pristine beam, usually of a few millimeters transverse size, in a 2D pattern, while the beam range is adjusted by changing the beam energy entering the nozzle (see later) [8]. The choice of the delivery technique has also a strong impact on the gantry design (see Section 1.2.5). This provides immense flexibility, confining the high-dose region entirely to the target volume without spilling into proximal normal tissue.

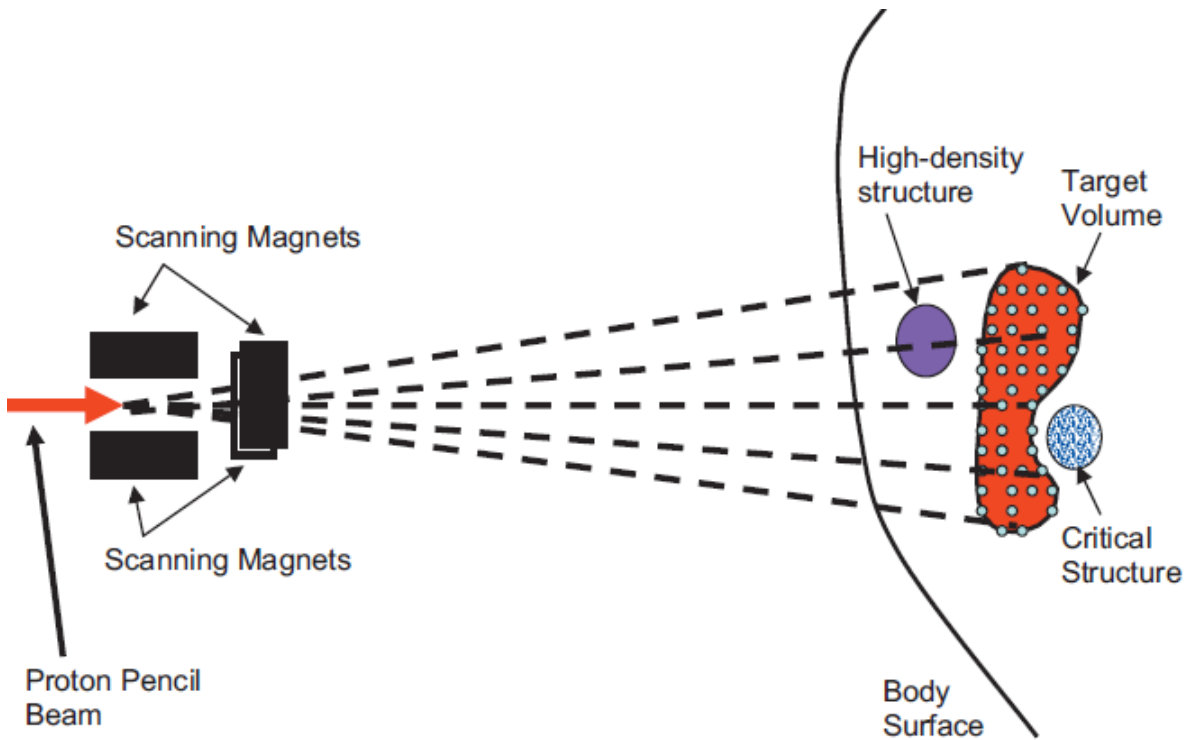


Figure 7: *Scheme of pencil beam scanning technique from [8]*

A treatment plan based on patient imaging is used to optimise the dose over the entire treatment volume, taking into account the dose both upstream and downstream of the Bragg peak delivered by a particular spot. Depending upon the largest intended treatment volume the scanning beam may need to address transverse fields up to 400 mm x 400 mm, although most facilities presently specify not more than 200 mm x 200 mm. In any case the treatment of very wide areas may be achieved by using the technique of field patching, in which the patient table is moved relative to the isocentre. The combination of pencil-beam spot scanning with a variable beam angle from a gantry enables the technique of intensity-modulated particle therapy (IMPT), in which several treatment fields (gantry angles) with inhomogeneous doses are combined to maximise the dose at the tumour and to minimise the dose to healthy tissue. IMPT involves active beam delivery devices and thus requires similarly fast and accurate dosimetry; typically only a few milliseconds can be budgeted to deliver the dose to a voxel (the single spot) if the total treatment time is

to be kept to a few minutes [11]. Other advantages of spot scanning are the elimination of patient-specific hardware, resulting in a patient setup faster and less costly, and a reduction in beam loss and hence neutron generation in the vicinity of the patient.

1.2.4 Accelerators for Proton Therapy

At present, nearly all hospital or laboratory centres use either a cyclotron or synchrotron as a particle source of either protons or carbon ions, delivering treatment beams to either single treatment rooms or (more frequently) multiple treatment rooms; in the latter case a transfer line and switching magnets are required to select which room receives beam. Both cyclotrons and synchrotrons are mature technologies with well-established routes for delivering maximum proton energies in the 200-350 MeV range or even higher. Currently, most proton accelerators in use are cyclotrons, while a smaller number are synchrotrons. However, new technologies are emerging to reduce facility costs and sizes [11]. In the following section, the main accelerator concepts used in proton therapy are described.

Normal-Conducting Cyclotrons and Synchrocyclotrons

The normal-conducting cyclotron was the first circular (and therefore cyclic) accelerator to be used, following its invention by Ernest Lawrence in the 1930s. A general scheme of a cyclotron can be found in Figure 8. There are a number of variants, which include techniques to keep the driving radio frequency acceleration in synchronism with the orbit period. Synchronism is achieved either by modifying the pole shapes to make the orbits isochronous, or by varying (in the synchrocyclotron) the Radio-Frequency (RF) during an acceleration pulse.

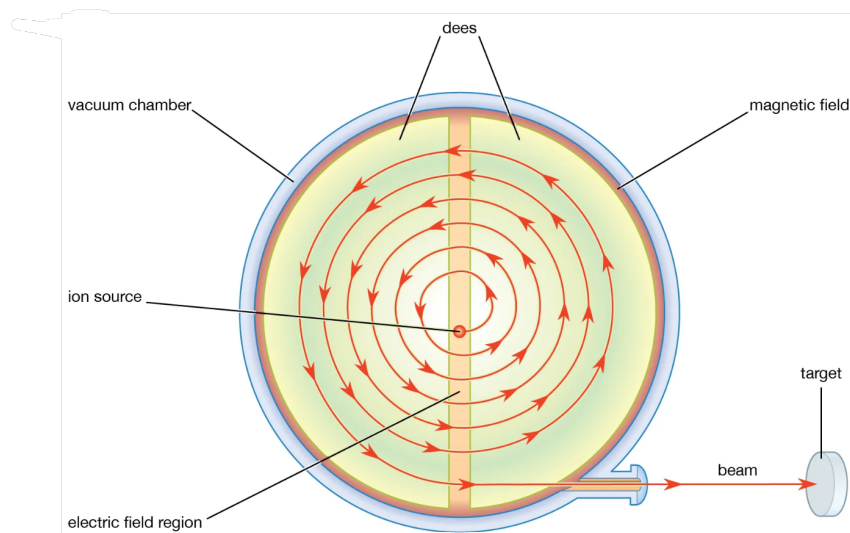


Figure 8: *Schematic illustration of a cyclotron*

Cyclotrons produce a continuous wave stream of protons, possessing a high and stable beam intensity perfectly suited for fast PBS repainting [8]. Protons are accelerated to

a fixed maximum energy so, to allow for depth scanning of the tumour, some method must be employed to vary the proton beam distal (maximum) depth. To achieve this variation in incident proton energy, the beam from the cyclotron is passed through an adjustable thickness of some material, typically two back-to-back wedges of carbon. The mean energy loss is accompanied by an increase in energy spread and beam emittance (the spatial spread of the beam) due to scattering, so the output beam must be cleaned in an energy-selection system (ESS) prior to the final beam delivery system. Energy selection is achieved with a combination of dipole magnets and collimators to select the energy and emittance of the beam that can be transported to the patient.

This mechanical degradation process, however, generates secondary neutrons and requires massive shielding. Typically cyclotrons can deliver sufficient beam intensity so that despite the beam loss from the energy selection process (by as much as a factor of one hundred or more for the lowest energies), they provide a dose rate that is competitive with other accelerator types. It is also worth noting that in typical cyclotron designs the output spot is basically circular, which simplifies the beam coupling to the final beam delivery system, for example to a downstream rotating gantry, since the coupling system is highly sensitive to 2D spot profile.

Superconducting Cyclotrons and Synchrocyclotrons

The higher fields (above about 3 T) which are available from superconducting magnets allow higher extraction energies at a particular orbit radius; this allows cyclotrons to be made smaller for a given extraction energy but with the penalty of the greater capital cost of the magnet and operating cost of the cryosystem. Reliability is not necessarily worse with a low-temperature rather than a room-temperature magnet, as in practice reliability is often determined by other points of failure. However, maintenance work on the accelerator will usually include a significant time overhead from warm-up and cool-down of cryogenically-cooled components. Several commercial vendors are now either developing or offering superconducting cyclotrons; Mevion utilise NbSn₃ superconducting magnet coils that allow the cyclotron to be small enough to be gantry mounted whilst maintaining a maximum proton energy of around 250 MeV. Varian-ACCEL use NbTi to have a larger, lower-field and therefore simpler magnet to obtain 250 MeV protons at extraction, whilst IBA also use NbTi in their 230-250 MeV S2C2 cyclotron. Superconducting magnets are often less than half the weight of their normal-conducting equivalent [11].

Synchrotrons

Synchrotrons are a well-established technology in proton therapy. At present, synchrotrons are the only accelerator technology used to provide carbon ion beams. Synchrotrons accelerate bunches of protons to the desired energy. A key feature is that each bunch can be accelerated natively to a different energy, which is advantageous for scanning techniques as it completely removes the need for external degraders, ensuring a cleaner beam with less shielding required [8]. However, they generally have a larger footprint and a lower, pulsed beam current. A picture of the synchrotron situated at CNAO (Italy) is showed

in Figure 9.



Figure 9: *Synchrotron at CNAO (Italy)*

All current designs follow the original approach by GSI and implemented at Heidelberg, which uses: an Electron Cyclotron Resonance (ECR) ion source, a radio-frequency quadrupole and drift-tube linac, and finally a synchrotron to accelerate carbon ions up to 400 MeV per nucleon. Energy variation of the proton or carbon beam distal (maximum) energy is accomplished by extracting the beam at different times in the acceleration cycle. Extraction is commonly achieved using either a third-order resonance or RF-knockout scheme and a feedback system is employed to ensure that the extracted dose can be controlled to provide both good dose stability and beam intensity that is programmable in time. Furthermore, extraction can be gated to synchronise the dose with the patient's breathing, in order to minimise the effect of organ motion.

In comparison with isochronous cyclotrons, where particles are continuously injected and accelerated, in synchrotrons (and similarly in synchrocyclotrons) the injection window is short, so the number of particles available at treatment energies is substantially lower. Nonetheless, dose rates are still adequate and in a synchrotron the available particle flux at each extraction energy is essentially constant; this is in contrast to cyclotrons, where the extracted beam intensity is reduced by up to three orders of magnitude by the scatterers used to reduce the mean particle energy.

Novel Accelerator Concepts

Even though the accelerator types described before are the most used clinically, some new designs are under study. For example, to overcome the limitations of traditional circular accelerators, next-generation facilities are exploring Fixed-Field Alternating-Gradient (FFAG) accelerators [11, 12].

Fixed-Field Alternating-Gradient (FFAG) accelerators combine the continuous operation of a cyclotron with the high-energy capabilities of a synchrotron. Like a cyclotron, an FFAG uses a magnetic field that is completely fixed in time but varies spatially (radially and azimuthally). However, its defining feature is the use of an alternating gradient

across successive dipoles, which provides strong focusing to keep the particle beam tightly controlled at higher relativistic energies. Two main configuration can be distinguished:

- **Scaling FFAGs:** The magnetic field varies non-linearly with the radius so that the particle orbit shape scales with energy. This maintains a constant "betatron tune" to avoid destabilizing resonances, but it requires massive, large-aperture magnets because the orbit radius expands greatly as the particles speed up.
- **Non-scaling FFAGs:** These use strong non-linear magnets to confine the beam to a much smaller physical aperture across a large energy range. While this allows for smaller, more practical magnets, the beam must safely cross resonances during acceleration.

By pairing these fixed, strong-focusing magnetic fields with fast swept-frequency RF cavities, FFAGs can accelerate particles in less than a millisecond. For medical applications, this working principle offers a major advantage: the potential for incredibly rapid, variable-energy beam extraction (delivering different energy pulses at rates up to 1 kHz), which would significantly speed up 3D tumor scanning compared to current technologies.

1.2.5 Proton Facility Layout and the Use of Gantry

In this section the main facility designs and beam transport techniques are illustrated. Starting with the different approaches toward the structure of a proton facility and the motivations behind them, the description of the main gantry architectures is given.

A single accelerator can provide a particle beam to a single treatment room or to multiple treatment rooms (see Figure??). Then in each room it is possible to find different configuration of how the beam is transported to the patient: if the beam comes from a fixed direction (horizontal/vertical plane) or from multiple directions thanks to the use of gantries as it will be described below. In most proton and carbon-ion systems today the particle source is located in a separate, static location and serves multiple treatment rooms. The advantage of having several treatment rooms supplied by a single accelerator is that patients can be prepared for treatment in parallel prior to irradiation, thus making optimal use of the available accelerator time. A possible complication may arise due to the risk of the accelerator source being the single point of failure for all treatment rooms, which must be taken into account. Moreover, such structures comprehend an extended network of beamlines, switching magnets, and a centralised degrader and ESS, together with a complex system of shielding resulting in a very big structure incompatible with integration into existing hospital buildings. Whilst the shielding requirements in all proton or carbon-ion facilities are naturally significant, particular attention must be paid in cyclotron-based facilities to the relatively larger amount of activation arising from the ESS.

Different approaches can be used to reduce the total size of the facility. In a single-room design, for example, it's possible to replace the large isochronous cyclotron, commonly

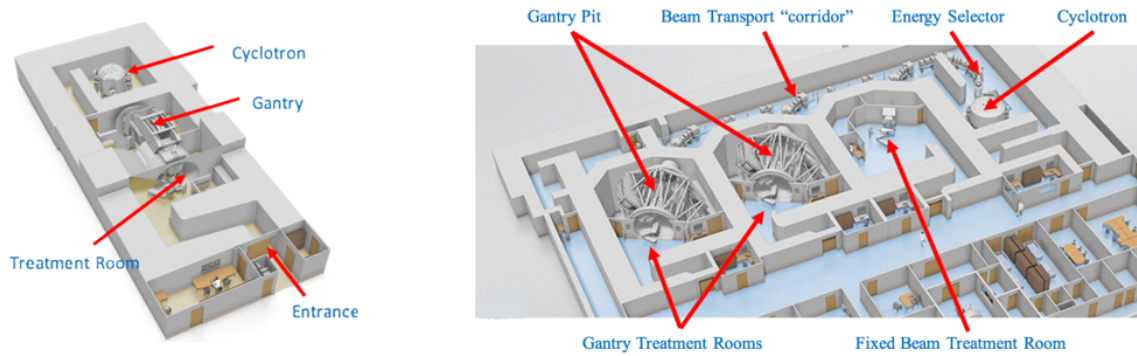


Figure 10: *Schemes of single-room design (left) and multiple-rooms design (right)*

used in a proton therapy center, with a superconducting synchrocyclotron (diameter 250 cm), roughly a factor of 1.7 reduction in accelerator diameter and a substantial reduction in mass, and relocate the degrader and ESS from a shared upstream vault to the entrance of the rotating gantry itself [12]. In this gantry-integrated ESS architecture, the beam extracted at a fixed energy travels only a short extraction beamline before reaching the gantry-mounted degrader, where energy selection occurs. Since all the elements are mounted on the gantry itself the radiation environment and shielding requirements are contained within a single room, reducing drastically the dimensions of the total structure, allowing also for single-room proton therapy in existing hospitals. A drawback of this approach is that, being all radiation sources co-located within the single vault rather than distributed across separate shielded areas, concrete activation is more severe and must be done close to the patient requiring careful shielding design even though the total shielded volume is dramatically smaller.

Another possibility to have a more compact systems addressed is to eliminate the upstream beamline entirely [11, 12]. The idea is to mount the accelerator directly on the gantry system, rotating together with the gantry, so no shared beamline is required. This is only possible if the accelerator is small and light enough that the resulting gantry is of reasonable size; of course in this scenario the accelerator can only support one treatment room. Superconducting accelerators must be used in order to reduce the size of the source and, in the case of a synchrocyclotron, the degrader can be directly substituted by a range shifter placed in the nozzle (see below) together with collimators. Because no upstream beamline exists, beam transmission from the accelerator to the patient is higher allowing to operate the accelerator at lower currents since there is no need to compensate for degrader losses.

The two previous approaches focus on how to reduce gantry-based facilities, but the gantry itself is the heaviest and largest component of these, thus, removing such an element has a strong impact on the total size. In gantry-less systems, the beam direction is fixed and the patient is repositioned using a robotic couch or upright support system; replacing gantry rotation with patient motion is mechanically simpler and cheaper but demands precise reproducible positioning and robust image guidance. A first strategy could be to retain the gantry-mounted synchrocyclotron but remove the rotation mechanism, leaving a fixed

horizontal beam modulated by the same nozzle-based range shifter. The patient is treated in an upright seated or standing position, constraining accessible tumour sites to those for which upright positioning is clinically and anatomically acceptable. The second strategy replaces the cyclotron-based accelerator with a compact synchrotron that extracts beam directly at the required clinical energy without any degrader, eliminating degrader-induced beam loss and secondary radiation entirely. The disadvantage is a sharply defined, narrow Bragg peak governed by the beam's intrinsic momentum spread rather than degrader straggling that requires more energy layers and more spots to cover a given target volume. Synchrotron energy switching is also slower than mechanical plate insertion, both effects increasing delivery time for the same target.

Gantry Architectures

Prior to the operation of the Loma Linda facility, treatments were carried out using both fixed beam lines and fixed patient orientation. Flexibility in the entry orientation of the beam is important since it allows to have the least possible impact on healthy tissues. Whilst static horizontal delivery is still preferred for some fields (such as ocular treatments) the capacity to provide an arbitrary entry angle is highly favoured by the medical community. Although it is acceptable to rotate or translate a supine patient in the horizontal plane, full six-dimensional patient motion is not possible. This is primarily due to the undesirable organ motion relative to the external body reference points used to align the treatment beam; thus horizontal rotation is acceptable but not other axes. Rotation may also be difficult for the patient, or interfere with other medical procedures such as anaesthesia [11]. Some treatments are suitable for use with fixed angle beam (which may be horizontal, vertical or something in between), with the patient either supine, prone or sitting up; a notable example is the treatment of ocular tumours where the patient is seated and the incident particle beam fixed and horizontal. However, to provide maximum flexibility the concept of the rotating delivery beam line (gantry) has been developed. Keeping the patient supine during radiotherapy treatment is useful to more easily reproduce the patient position used for pre-treatment imaging such as CT that has been used for treatment planning and to more easily reproduce the patient position through several weeks of daily treatment. In external beam radiotherapy by far the most common method is for the patient to lie on a treatment couch, imitating the position used for CT scanning. When accompanied with sensible immobilisation devices, this ensures organs are in similar position during both treatment planning and treatment, to give a reproducible set up.

Conventionally, the term gantry is used to refer to a particle beam transport line that is designed to rotate around an axis; a gantry consists of a mechanical support structure, drive mechanism, magnets, vacuum vessels and beam diagnostics, along with other secondary technical infrastructure [11]. Three main gantry architectures have been developed:

- **Isocentric Gantries** represent the standard design wherein the patient is kept essentially still in a prone position with the centre of rotation of the gantry passing in the horizontal plane through the patient and the incident beam rotated in the vertical plane around the patient (see Figure 12). A number of dipoles are used

to transport the beam from the particle source to the treatment room which it enters along this axis. Further dipoles on the gantry are used to create an offset between the beam and the gantry rotation axis and finally turn the beam toward the patient who is positioned at the isocentre. The components between the final bending magnet and the exit window to the patient are sometimes referred to as the treatment nozzle (see Figure 11).

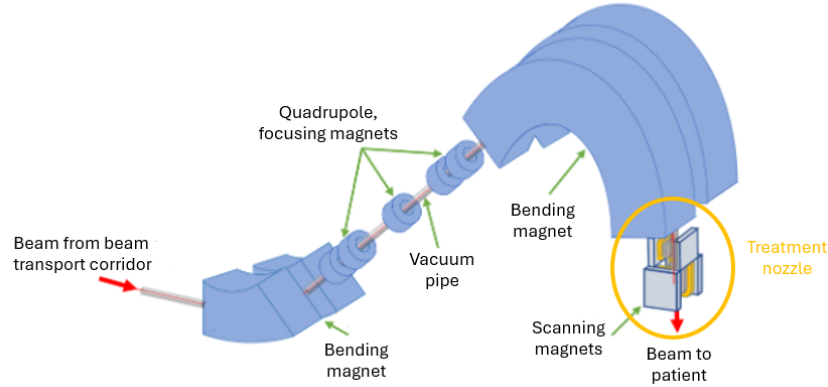


Figure 11: *Schematic illustration of beam transport in a gantry design and treatment nozzle*

As well as beam position and dose monitors it may include deflection magnets to scan the spot transversely, or alternatively beam scatterers and collimators to spread and shape the proton dose across a chosen field size; The need for a treatment nozzle will always require a distance of several metres between the last bending magnet of a gantry and the patient. To obtain a full 4π coverage of the patient, the gantry must rotate at least 180° in conjunction with a patient table that rotates 360° in the horizontal plane. To minimise patient rotation (which introduces time delay and may result in unacceptably large patient misalignment) many gantry designs utilise the full 360° of rotation around the patient.

- **Riesenrad Gantries** is an alternative approach that has been proposed to reduce the mass of moving steel. The heaviest component of a gantry is the bending magnet. In this riesenrad design (called also ferris wheel) some deflecting magnets lie on the gantry rotation axis so the weight of the moving part is reduced. The patient is moved then around the rotation axis (but kept supine) so the dose is delivered from different angles. The Riesenrad gantry is shown schematically in Figure 13. Such gantries have less moving steel and are therefore lighter, but have more complex patient-handling issues compared to isocentric gantry installations; the principal of these is that reaching the patient in case of emergencies, like a cardiac attack, is more time-consuming and so an issue.
- **Eccentric Gantries** represent an hybrid scheme that has been implemented at Gantry 1 at PSI (see Section 2.3), in which both the patient and the beam line magnets move around the rotation axis, thus minimising the overall diameter of the gantry. Furthermore, it requires a smaller shielded room than the riesenrad design.

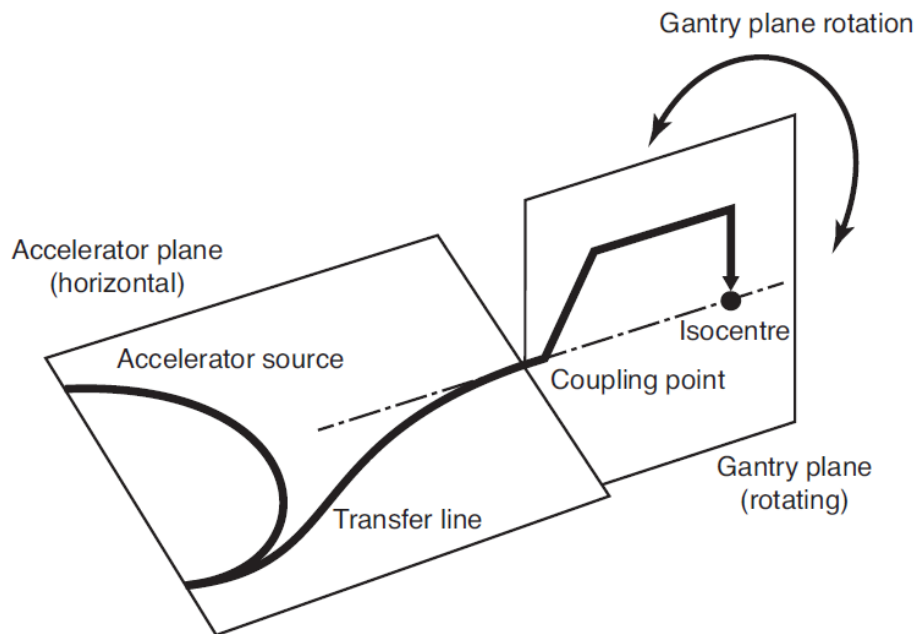


Figure 12: *Schematic illustration of Isocentric gantry.*

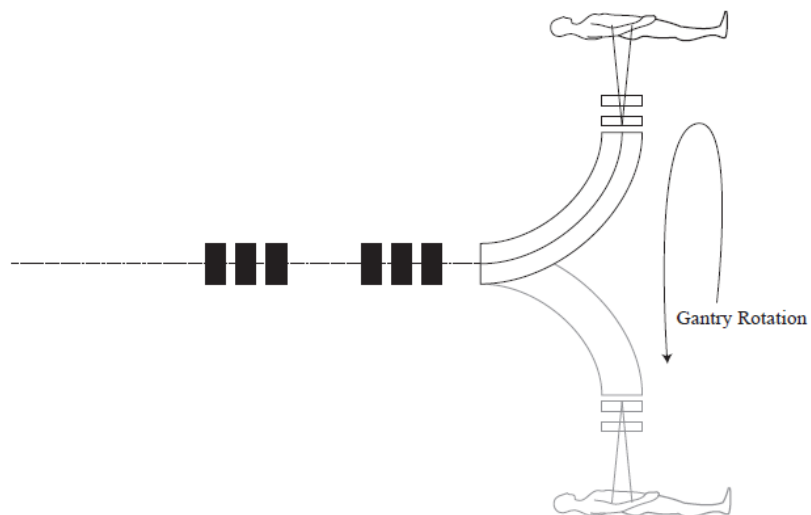


Figure 13: *Schematic illustration of Riesenrad gantry.*

As already said, the most used design is the isocentric one. At this point another distinction can be made for isocentric gantries in the case of the PBS technique. In most current treatment nozzle designs, the pair of fast-scanning deflection magnets are mounted after the final dipole (*downstream*), as shown in Figure 14. An important figure of merit in

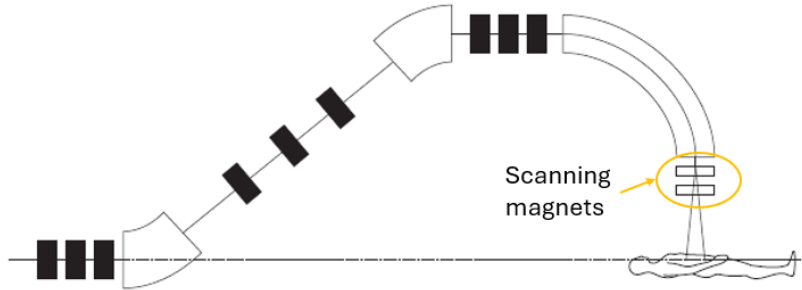


Figure 14: *A schematic illustration of an isocentric gantry which incorporates spot scanning magnets downstream of the final dipole.*

pencil-beam spot scanning is the source-to-axis distance (SAD) [11], which is the distance from the isocentre to the apparent source of the particle beam. If there are no beam focusing elements between the scanning magnets and the isocentre, the effective source location is the point at which changes to the angle of the beam are made, i.e. the location of the scanning magnets. Since the beam trajectories diverge from the source, the area intercepted at the patient's skin will be smaller than the area at the isocentre depth, and thus a higher dose will be delivered to the skin. Making the SAD as large as possible will therefore give the best degree of skin sparing and uniformity of dose distribution. There are two methods by which the SAD may be made either very large, or even infinite. The first is to have two pairs of fast-scanning deflection magnets, instead of just one pair as for the standard downstream configuration, mounted after the final dipole which could produce a parallel beam translation at the patient surface; this either requires a large distance from the final dipole to the patient to develop the lateral spot offset, which demands a larger gantry radius, or very technically demanding scanning magnets. The second approach is to have either one or both of the fast-scanning deflection magnets *upstream* of the final dipole; this scheme is shown schematically in Figure 15. The beam

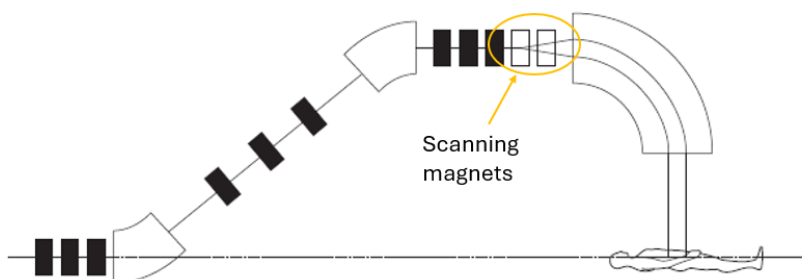


Figure 15: *A schematic illustration of an isocentric gantry which incorporates spot scanning magnets upstream of the final dipole.*

optics can then be designed such that the beam leaving the final dipole is translated

parallel to the zero-deflection axis. In this upstream scheme the gantry radius does not need to be increased to include scanning; however the good field region (and therefore the magnet pole width and the pole gap) of the final dipole must be increased to allow for the transverse beam displacement required to produce the chosen treatment field size, which adds significantly to its weight. The first example of a parallel scanning gantry was PSI Gantry 2, implemented in 1996 (see Section 2.4).

1.3 Motion Mitigation in PBS

Despite its dosimetric superiority, PBS introduces a severe vulnerability when treating moving targets (e.g. lung or liver tumours). Motion represents a fundamentally spatiotemporal limitation on dose delivery, that has been acutely exposed by the transition from passive scattering to PBS [12].

Because PBS constructs a three-dimensional dose distribution sequentially over time, it is intrinsically sensitive to any anatomical displacement occurring between the delivery of successive spots or energy layers. In thoracic and abdominal tumours, where respiratory motion continuously modulates both target position and water-equivalent path length, this sensitivity is clinically decisive. A tumour that moves 15-20 mm with each breathing cycle represents a difficult target to be irradiated. The governing physical phenomenon is the interaction between tumour motion and the temporal sequence of spot-by-spot, layer-by-layer dose delivery. Because individual spots are deposited at different moments across a delivery that may span tens of seconds, the dose actually received by any given tissue voxel depends not only on the planned spot weights but on where that voxel happens to be each time the beam passes through its depth range. The resulting dose distribution is a probabilistic function of the relative phase between beam delivery and breathing motion.

Some clinical strategies address this problem indirectly by modifying delivery conditions rather than eliminating the temporal mismatch itself. *Rescanning* delivers dose in multiple sub-fractions so that motion-induced inhomogeneities average across breathing cycles, but each additional pass multiplies delivery time by a factor of four to eight [12]. *Respiratory gating* restricts delivery to a 30-40 % window of the breathing cycle, extending treatment time by a factor of two to three. *Breath-hold* suspends respiratory motion but is limited by patient breath-hold, duration—typically 5-15 seconds, which is often shorter than the time required to deliver a full PBS field, necessitating multiple interrupted deliveries. In practice these strategies are frequently combined, extending treatment sessions for thoracic and abdominal tumours to 30-45 minutes per fraction. Every current mitigation approach accepts the fundamental constraint of slow delivery. A direct solution would be to have field delivery that could be completed within a single comfortable breath-hold of 5-10 seconds, avoiding the problem, rescanning would be unnecessary, and gating replaced by a brief breath-hold compatible with nearly all patients [12].

Improving treatment efficiency would also maximize beam utilization and patient throughput apart from addressing the motion problem. Reducing total field delivery time is therefore a defining technical objective for the current generation of proton therapy systems, one with simultaneous implications for motion management, patient throughput,

and cost. The total delivery time of a proton therapy field divides into two categories: *beam-on time*, during which dose is actively deposited, and *dead time*, comprising energy layer switching and spot transition overhead. A meaningful reduction in the total treatment duration should optimize each one of these components. Below, the main strategies are described:

- **Beam-on time:** Beam-on time is directly proportional to the dose per fraction and inversely proportional to the achievable beam current at the isocenter. Clinical constraints, including minimum monitor unit requirements per spot and the need to maintain beam quality across the full clinical energy range, converge on a target of approximately 5-10 nA at the patient location. Reaching this target in gantry-based remote-ESS systems requires overcoming the substantial transmission losses incurred during energy degradation (see Section 1.2.4, 1.2.5). Three strategies have been validated to raise isocenter current toward this range.

The first is degrader material optimization. Low-scattering materials such as boron carbide and beryllium generate less multiple Coulomb scattering than conventional graphite, limiting emittance growth at the degrader and improving downstream transport efficiency. The second is asymmetric collimation. Conventional circular collimators select equal emittances in both transverse planes, but the alternating focusing of quadrupole and dipole elements in a clinical beamline creates inherently different acceptance limits in the horizontal and vertical planes. Asymmetric collimators that independently optimize beam size and divergence selection in each plane exploit this structural asymmetry, increasing phase-space transmission through the energy selection system by factors of 5-6 for low-energy beams. The third strategy is large momentum acceptance beamlines, which relax the precision required of momentum selection and allow a wider phase-space volume to reach the patient, combined with momentum cooling, an emittance-exchange technique in which a wedge-shaped low-Z absorber replaces the conventional ESS slit, reducing the beam momentum spread without discarding particles and enabling order-of-magnitude improvements in transmission for the lowest clinical energies.

- **Spot transition time:** Spot transition dead time accumulates across the full set of lateral beam positions in an IMPT field. Although individual transitions take only a few milliseconds, their cumulative contribution is significant across the thousands of spots in a clinical plan. Two classes of intervention directly reduce this component.

At the treatment planning level, spot-reduction algorithms iteratively remove low-weight spots while maintaining dosimetric quality constraints, consistently reducing spot counts by 30-50 % with equivalent or improved target coverage and organ-at-risk sparing. At the delivery level, line-scanning and continuous scanning approaches replace discrete spot irradiation with a continuously moving beam, eliminating lateral transition events and reducing spot transition time to approximately 2-3 seconds per field in both cyclotron and synchrotron-based implementations. Synchrocyclotron-based systems offer a structural advantage in this regard: the pulsed beam structure, with beam-off intervals of approximately 1-1.3 ms between extraction pulses, allows scanning magnets to reposition asynchronously during beam-off intervals without contributing to delivery time, effectively decoupling spot

transition overhead from the time budget. Through these combined approaches, total spot transition time can be confined to 2-3 seconds per field.

- **Energy layer switching time:** Energy switching time varies from approximately 0.5 seconds in direct-ESS to 2 seconds or more in conventional facilities, depending on accelerator type. This variability reflects fundamentally different physical constraints: mechanical range shifter plates operate on timescales set by motor dynamics, while magnetic energy selection in remote-ESS is governed by magnet inductance and beamline response, and synchrotron energy ramping is limited by ring magnetic field cycling. The most broadly applicable strategy for reducing cumulative energy switching dead time is to reduce the number of energy layers required to cover the target, rather than the per-layer switching speed alone. In multi-energy extraction from a synchrotron, energy switching times can be as low as 0.2 seconds. Ridge filters achieve this by broadening the individual Bragg peak depth-dose distribution, allowing a single energy setting to span a greater depth range and directly reducing the number of layer transitions required. Multiple ridge filter designs have been developed and validated across proton and ion beam systems, including mini-ridge filters, two-dimensional ripple filters, and dynamic variants in which broadening can be modulated within a single delivery. Dynamic ridge filters apply maximum broadening where it is dosimetrically safe, interior target voxels, while reverting to minimal broadening for peripheral and distal layers where sharp dose fall-off is required to spare adjacent structures, removing the historical trade-off between delivery speed and dose conformity.
- **Combined optimization:** Integrating these hardware and algorithmic optimizations across all three delivery time components, total field delivery times of approximately 10 seconds become achievable even for large tumour volumes. Such rapid delivery enables treatment within a single breath-hold, eliminating the need for time-consuming respiratory gating and substantially improving patient throughput.

Fast delivery approaches combining different accelerator architectures and planning techniques have been experimentally validated across two representative clinical platforms. At PSI's Gantry 2 (see Section 2.4) combined high-transmission beam optics and spot-reduced treatment planning demonstrated single-breath-hold delivery for locally advanced NSCLC (Non-Small Cell Lung Cancer) cases, achieving field delivery times below 10 seconds for conventional fractionation and below 15 seconds for hypofractionation [12]. At Stanford Medicine, the Mevion S250-FIT, the most compact upright proton therapy system in clinical operation, demonstrated full-field delivery for lung cancer within a 5-10 second breath-hold using software-only optimizations requiring no hardware modifications. Together, these results confirm that sub-10-second delivery is achievable across fundamentally different system architectures.

1.3.1 Proton Therapy around the Globe

Over the last two decades, there has been explosive growth in proton centers globally. According to PTCOG [13], the number of centers has increased from 52 in 2015 to 128

today, with projections approaching 200 by 2031. However, despite this expansion, less than 1% of radiotherapy patients worldwide are treated with protons, while the vast majority (approximately 90%) receive photon radiotherapy (IMRT/VMAT).

The primary bottleneck is not clinical evidence, but rather cost and complexity [12]. The high cost of proton therapy is rooted in the physical requirements of generating and controlling high-energy charged particle beams. Clinically relevant treatment depths require proton kinetic energies spanning 70-230 MeV. At a fixed energy, the magnetic rigidity determines the scale of every component. In the fundamental relation:

$$B\rho = \frac{p}{q} \tag{10}$$

where B is the magnetic field strength, ρ is the bending radius of the particle's path, p is the particle's momentum and q is the charge, it is possible to see that bending a high-momentum proton beam requires either stronger magnetic fields or larger bending radius. In practice, this translates into rotating gantries that have massive size and are incredibly heavy imposing substantial mechanical complexity and driving the need for large treatment rooms and their supporting structures. As already seen (Section 1.2.5), modern physics-driven innovations are shifting toward compact, single-room architectures, gantry-mounted accelerators, and upright patient positioning.

Another way to reduce the cost of proton therapy is to reduce the treatment time itself. This increases patients treatable per day, improves machine utilization and lowering cost per fraction [12]. In Section 1.3 some example on how to reduce the total delivery time were described.

All these new approaches are contributing to narrow the gap between conventional radiotherapy and proton therapy with direct impact on the quality of patient's treatments.

2 CPT Facility and Gantry 2 at PSI

In this chapter, an overview of the Center for Proton Therapy (CPT) at the Paul Scherrer Institute (PSI) is given. In particular, Gantry 2 is described, where all the data acquisition campaigns described in the following chapters have been performed.

2.1 Historical Background and the PROSCAN Project

The Paul Scherrer Institute (PSI) has a long-standing and successful history in the development and application of particle beams for cancer treatment. From 1981 until 1992, the institute utilized pion therapy, successfully treating more than 500 patients with a highly advanced scanning technology. However, pion therapy was ultimately abandoned in 1992 in favor of light ions, leading to the development of the world's first scanning gantry for proton therapy (Gantry 1) [14].

The success of the initial proton therapy programs, coupled with novel technical developments in intensity-modulated proton therapy (IMPT), led the PSI directorate in the year 2000 to launch a major facility expansion known as the PROSCAN project. The overall objective of PROSCAN was to implement a base technology laboratory for the advancement of proton therapy, preparing the compact gantry system for a transfer into a marketable product for hospital applications. The PROSCAN expansion included (see Figure 16) the installation of a dedicated commercial superconducting cyclotron, the construction of new beamlines, the realization of a second-generation scanning gantry (Gantry 2), a new eye-treatment facility (Optis 2), and subsequently a third gantry (Gantry 3).

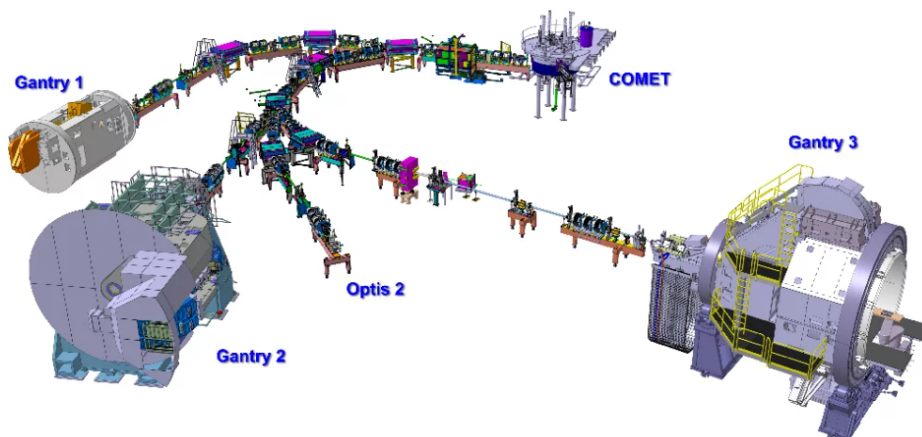


Figure 16: *Layout of the PROSCAN facility beam lines*

2.2 The Accelerator: COMET Cyclotron

The core of the PROSCAN facility is a dedicated superconducting cyclotron named COMET (COmpact MElical Therapy cyclotron) able to accelerate protons up to 250 MeV of kinetic energy. The accelerator was built by the company ACCEL Instruments GmbH (Germany) in strong collaboration with PSI, based on an original design by Prof. H. Blosser of Michigan State University, and was installed at PSI in 2007 [14]. This was a prototype of accelerator which has been commercialized afterwards.



Figure 17: *The COMET superconducting cyclotron at the PSI PROSCAN facility.*

The accelerator (see Figure 17), which has a diameter of 3.2 meters, contains an ion source in which hydrogen atoms are continuously split into negatively charged electrons and positively charged protons in fractions of a second. An electric field draws the protons into the cyclotron. There, the protons rotate 630 times on a spiral circular path before being extracted into a vacuum tube with the help of electric fields. In the tube, the protons are bundled into a 5 to 7 mm wide beam by magnets on the outside and guided at 61% of the speed of light about 50 meters to one of the therapy facilities. A kicker magnet at the output of the cyclotron is used to switch the beam on and off quickly. The switching time is 200 μs from the trigger signal of the therapy control system to the disappearance of the beam signal at the treatment site. Additional switch-off elements (safety functions) include the reduction of the cyclotron high frequency, the switching off of the ion source, and several mechanical beam stoppers [15].

The cyclotron delivers a stable continuous wave (DC) beam that is optimally suited for pencil beam scanning. The intensity of the beam can be adjusted at the ion source from below 1 nA up to an extracted maximum of 850 nA. For clinical use on Gantry 2, the average proton current is typically maintained between 200 and 400 nA. A critical component of the COMET cyclotron is a vertical deflector plate located in its central region, which acts on the first orbits of acceleration. By varying the electric field of this plate, the intensity of the extracted beam can be modulated dynamically from 0 to 100% in approximately 0.1 ms.

Because the cyclotron extracts protons at a fixed energy of 250 MeV, a degrader system is

required to achieve the lower energies necessary for treating variable tumor depths. The extracted beam is focused onto a fast degrader consisting of a multi-wedged B_4C absorber. This system can rapidly insert variable amounts of material into the beam path, decreasing the proton energy to any value in the therapeutic range of 70 to 230 MeV. The degrader is immediately followed by collimators and an energy selection system (an achromatic bending section with momentum analysis slits) that restores the beam quality, defining a well-controlled beam emittance (max 30 mm mrad) and a momentum spread of $\pm 1.0\%$.

2.3 Gantry 1: The First Scanning Gantry

Inaugurated in 1996, Gantry 1 was the first gantry in the world dedicated to pencil beam scanning. It was designed with a highly compact layout featuring a radius of only 2 meters. To achieve this compactness, the patient table is mounted eccentrically (see Section 1.2.5); it is physically attached to the gantry and rotates with it, utilizing a counter-rotation mechanism to maintain the patient in a horizontal position at all times [16].

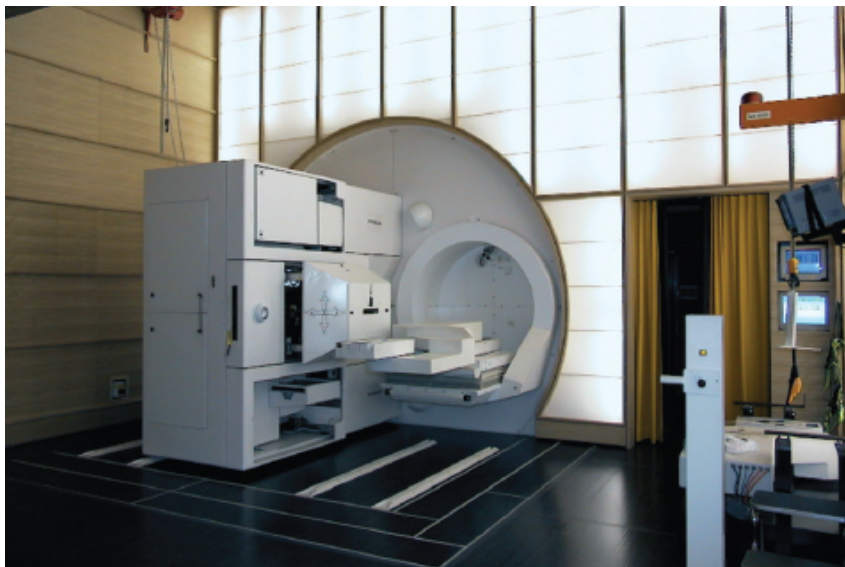


Figure 18: *Gantry 1 at PSI, featuring the eccentric patient table mounting.*

Gantry 1 employs a discrete "step-and-shoot" spot scanning method using a proton pencil beam with a Gaussian profile of 7-8 mm FWHM, scanning in steps of 5 mm. Originally, with Gantry 1, only non-moving targets could be treated due to possible interference between the target motion and the dynamic motion of the pencil beam, which can produce substantial errors in the homogeneity of the dose distribution within the target. The magnetic scanning on Gantry 1 was applied in only one lateral direction (the dispersive plane, U) using a single sweeper magnet. The second scanning dimension (depth, S) is controlled by a range shifter system located in front of the patient, consisting of a stack of 5 mm-thick polyethylene plates moved pneumatically into the beam. Currently, Gantry 1 is used only for experiments and, for this reason, the second scanning direction was commissioned over the range of ~ 5 cm which is suitable for small animal irradiations.

It is important to briefly explain the reference systems used for proton treatments at PSI. As can be noticed from the previous paragraph, the scanning directions are called T , U , and S . This is primarily to avoid confusion with the fixed room or patient coordinate systems. When dealing with a rotating gantry, things can get mathematically confusing very quickly. The patient lies on a table in a fixed room, which is typically mapped using standard X, Y, Z coordinates. However, the gantry (and the beam) is constantly rotating around the patient. To keep the physics calculations clear, the PSI team uses a separate, local coordinate system (T, U, S) that is physically attached to the rotating nozzle of the gantry:

- S -axis: This is the longitudinal axis, representing the direction the proton beam is traveling straight out of the nozzle (the depth dimension into the patient).
- T -axis: This stands for the Transverse direction. Specifically, it represents the axis that lies inside the bending plane of the gantry's large dipole magnets.
- U -axis: U is simply chosen as the adjacent alphabetical letter to represent the second transverse axis. It is strictly orthogonal to both T and S (meaning it points perpendicular to the gantry's bending plane).

In the following chapters, the T , U , and S coordinates are often used instead of the more common X , Y , and Z coordinates.

2.4 Gantry 2: Next-Generation Scanning System

Gantry 2 was developed as a second-generation system specifically designed to overcome the limitations of Gantry 1, primarily aiming to increase scanning speed to allow for volumetric repainting of moving targets.

2.4.1 Mechanical Layout and Isocentric Design

Unlike its predecessor, Gantry 2 utilizes an isocentric layout (see Section 1.2.5). The rotating beamline is supported by a central commercial pivot bearing located before the last bending magnet, leaving the treatment room comfortably large and permanently accessible on a fixed floor. The parallel displacement of the beam axis from the central rotation axis of the gantry was chosen at a distance of 3.2 m. The diameter spanned by the mechanical system of the new isocentric Gantry 2 is about 8.4 m. The distance of the beam exit of the last 90° bending magnet to the isocenter is 1.7 m, which keeps this component outside of the half-cylinder cell of the treatment area [14]. The mechanical systems (gantry support and patient table) were delivered by the Swiss company Schär Engineering Ltd. The other gantry components were realized internally at PSI.

An unusual feature of the system is the limited rotation of the gantry, which ranges from -30° to +180°. The gantry, therefore, rotates only on one side. The patient table is



Figure 19: *Gantry 2 treatment room layout showing the isocentric design and fixed floor setup, together with the in-room CT.*

mounted on the opposite side (i.e., along the beam axis when the gantry is horizontal at a gantry angle of $+90^\circ$). The original goal was to design a treatment room that looks like a standard square room, with the exception of the half-cylindrical wall where the nozzle rotates from 0° to 180° , in order to conceal the gantry, leaving only the nozzle visible. Later, to allow for faster selection of treatment angles when treating with a beam from above, the rotation range was extended to -30° . The trade-off is a mechanically more complex and costly system. The flexibility to choose any desired beam incidence is achieved by rotating the patient table in the horizontal plane.

By not having a full rotation of the last 90° bending magnet, it is possible to avoid the usual problems of having an open gantry pit in the area at the isocenter. A fixed "false floor" is present in the treatment room, which is supported from the outside of the gantry pit and is not "cut" by the rotation of the gantry head. In this way, easy permanent access to the patient table at any time can be provided, with the exception of the slit region where the nozzle rotates, which is covered by a rolling floor. The fixed walls and a (partial) fixed ceiling in the vicinity of the isocenter permit the mounting of commercial diagnostic equipment in a fixed environment at the isocenter, e.g., planar lasers for marking the isocenter, devices for stereo viewing of the patient surfaces, etc. The limited rotation of the gantry also allows supporting the gantry in the central region with a commercial pivot bearing. By doing this, PSI avoided the use of an 8 m large cylinder as a gantry support, which is difficult to fabricate to the required precision. A picture of the Gantry 2 treatment room is shown in Figure 19.

2.4.2 Equipment for Patient Positioning and for Image Guided Proton Therapy

- **Patient table** The patient table was provided by Schär Engineering Ltd. The table is set on a vertical carriage at a distance of about 1.8 m from the isocenter. A first translational axis, Y, moves the whole patient table vertically up and down over 70 cm. A pivotal axis ϕ on top of the vertical carriage provides the main central rotation of the upper part of the table. On top of the rotation ϕ -axis, a radial support moves over a length of 2.6 m providing the second translation axis, L. A second rotational axis Ω , which can rotate by $\pm 141^\circ$, is mounted at the end of the radial support. On top of the Ω -axis is the clamping mechanism for mounting the actual patient support (the couch), which can be of different types and sizes and can be exchanged. The individual patient moulds are clamped on the couch support [14].

Through the combination of the two rotations and one longitudinal translation of the patient table in the horizontal plane, it is possible to treat the patient in a supine position with the tumor at the isocenter for all horizontal beam angles in a range of about $\pm 120^\circ$ with respect to the main patient body axis. Including the gantry rotation, the degrees of freedom for choosing the beam incidence on the supine patient cover a solid angle of more than 2π . Indeed, it is not required to cover the whole 4π solid angle since the beam incidences of interest are those with an entrance point in the patient's body sufficiently near in proton range to the tumor location. The patient table offers also the possibility to orient the patient and the tumor in a favorable position with respect to the beam and to apply pitch and roll corrections to the patient couch.

A major requirement for the mechanical systems has been the ability to move the gantry and the patient table under remote control. This brings the freedom to deliver dose fields sequentially without the need for personnel to enter the room between fields. As a consequence, it is required to guarantee patient safety against possible mechanical collisions through automation. This has been realized using dedicated safety hardware with collision detection devices and software with "virtual walls" limiting the regions of the possible movements of the table. The software for controlling the mechanical devices for the positioning of the patient table and the gantry is being developed internally by PSI engineers.

- **Sliding CT** The layout of the gantry was conceived for maximum flexibility, permitting the installation of a sliding CT, which can be observed in Figure 19. The idea was to be able to install in the treatment area the best commercial diagnostic equipment available on the market, to be used within reach of the patient table, to check with the highest precision the setup of the patient before and after beam delivery. The possibility to take time-resolved images is of particular interest for treating tumors in the context of moving organs, for developing new quality assurance methods, and for supporting the patient setup for gating, tracking, or breath-hold techniques.
- **BEV X-ray** The last 90° bending magnet has been designed with a hole in the external return yoke, which allows shining X-rays through the last 90° magnet along

the nozzle. On the gantry, a retractable support is mounted, allowing the positioning of an X-ray panel behind the patient for taking X-ray and fluoroscopy images. This system takes images in the direction of the proton beam (Beam's Eye View, BEV), providing increased precision and quality assurance, in particular in the treatment of moving tumors.

2.4.3 Upstream Scanning System

Gantry 2 is an "upstream scanning" system, meaning the two sweeper magnets (W_T and W_U) are installed before the last 90° bending magnet (see Section 1.2.5). This compacts the gantry radius by saving drift space after the final bend. This is the same solution used with Gantry 1, but with two sweeper magnets instead of only one. By using a solution with upstream scanning, it is possible to provide parallel beam scanning in both lateral scanning directions. The advantages of using a parallel scanned beam were already listed in the previous chapter. This simplifies treatment planning and dosimetry. The dose distributions delivered in the patient and in the dosimetric systems are very similar, independent of the longitudinal position of the equipment along the beamline, permitting less skin dose and avoiding dose homogeneity errors due to longitudinal dose distortion effects. The T-sweeper deflects the beam transversely over ± 6 cm, while the U-sweeper deflects the beam in the dispersive plane over ± 10 cm, yielding a nominal scan area of 12×20 cm at the isocenter.

To maintain a parallel and focused beam across this entire scan area, despite the different path lengths through the final bending magnet, several beam optics corrections are employed. A tapering was applied to the poles of the U-sweeper, and a dynamic thin quadrupole corrector (Q_C) was connected in series with the U-sweeper to correct focal plane tilting. The overall layout of the gantry beamline, which is shown in Figure 20, consists of three dipoles (elements A) and seven quadrupoles (elements Q). In a beamline the quadrupoles are used to focalize the particles while the dipoles are used to curve and change its direction.

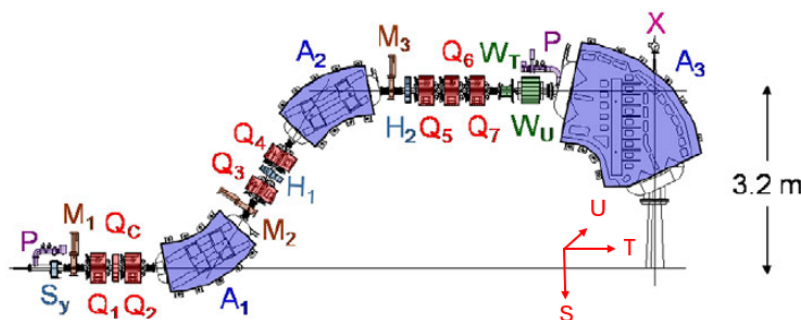


Figure 20: *The elements of the Gantry 2 beam line [14]. Elements A_{1-3} are dipoles, $Q_{1-7,C}$ quadrupoles, W_T , W_U sweeper magnets used for scanning, M_{1-3} profile monitors, P vacuum pumps, S_Y steering magnet, $H_{1,2}$ sextupoles. X is the location of the X-ray tube.*

All magnets were designed by the magnet group of PSI and fabricated by industry

(Sigmaphi). A major goal was to achieve very fast changes of the beam energy in the beamline, as better described in Section 2.4.5.

Another important feature to note is that the beam is injected into the gantry with a symmetric phase space in order to obtain an invariant beam transport through the gantry, independent of the gantry rotation.

2.4.4 Nozzle Structure and Instrumentation

The nozzle of Gantry 2 was meticulously designed to minimize material in the beam path to prevent multiple Coulomb scattering, achieving a sharp pencil beam width (sigma) of less than 3 mm at most energies, and under 5 mm even at the lowest energy of 70 MeV [14].

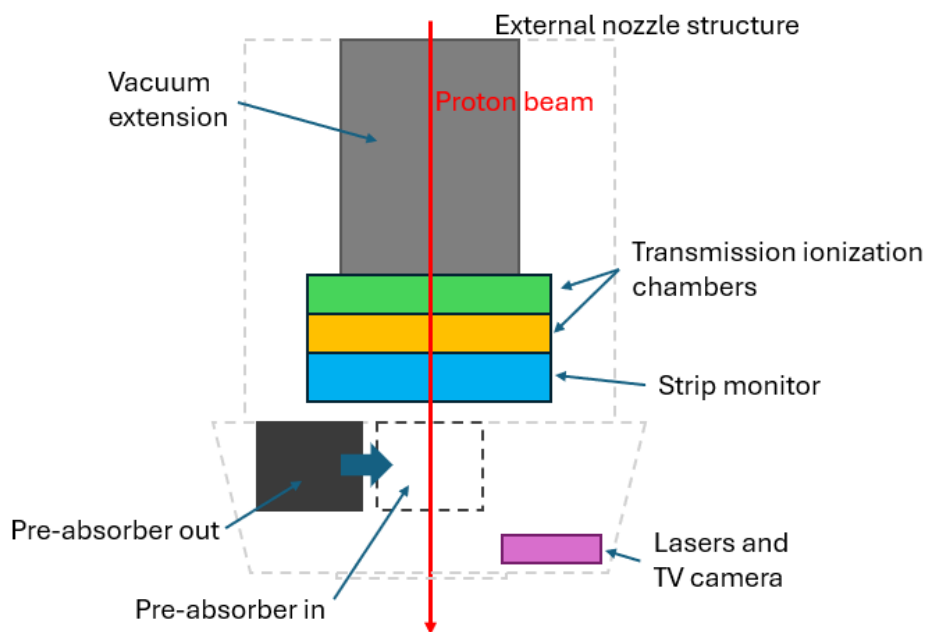


Figure 21: *Simplified scheme of the Gantry 2 nozzle, highlighting the vacuum extension, monitors and pre-absorber block.*

The main features of the nozzle are the following:

- **Vacuum extension** The vacuum chamber of the last bending magnet extends into the nozzle in order to minimize beam scattering, allowing for the narrowest pencil beam possible. This also serves to reduce the distance from the vacuum window to the isocenter, which in this case is about 90 cm, further reducing beam scattering caused by air and other materials in the nozzle.
- **Beam monitors** Within the nozzle, two transmission monitors, M1 and M2, are mounted. These plane-parallel ionization chambers measure the instantaneous intensity of the pencil beam and are calibrated to the number of delivered protons.

They are used to control the amount of delivered dose on-line. A strip monitor (an ionization chamber with 2 mm wide strips in the T and U directions) is mounted in the same box. The chamber was fabricated and delivered to PSI by the University of Torino in the framework of a collaboration with the TERA group in Italy. This monitor is used for measuring the position and shape of the pencil beam in front of the patient during beam delivery. These monitor elements are contained in an insulated box, attempting to provide an optimally shielded environment against electrical noise, sound, and mechanical vibrations. All these monitors provide the number of Monitor Units (MUs), related to the number of protons delivered, that were used for the data analysis described in Chapter 5.

- **Pre-absorber** Underneath the detector box is a support, which allows a block of graphite, with a water equivalent thickness (WET) of about 4.2 cm, to be moved in and out of the beam under remote control. This block is used to deliver shallow proton ranges to the patient that are not available in the standard beam tune range, usually energies below 70 MeV. The insertion of the pre-absorber results in a general broadening of the spots delivered and must be taken into account, as can be seen in Chapter 5.
- **Laser and TV camera** A TV camera and a set of lasers are also mounted laterally outside of the scan area, used for viewing the alignment of the patient on the beam axis from within the nozzle.
- **Longitudinal nozzle motion** The entire nozzle, including the monitors and the elements below them, can be moved along the beam direction under remote control over a distance of 27 cm. This motion is used to reduce the air gap between the patient and the nozzle, while keeping the tumor and the patient at the isocenter, where the beam is best focused.
- **Collision detection** The entire gantry system, like every element in the room, is protected against mechanical collisions by a collision detection system. As mentioned previously, this allows the gantry, the patient table, and the nozzle elements to be moved under remote control to deliver several fields in sequence without personnel entering the room.

2.4.5 Beamline Integration for High-Speed Scanning

The advanced scanning capabilities of Gantry 2 rely heavily on the design of the upstream PROSCAN beamline. While the gantry's sweeper magnets control the transverse position of the beam, the temporal structure and depth of the dose deposition are governed by three high-speed components located upstream:

- **Vertical Deflector Plate:** Located in the central region of the cyclotron, this component can dynamically modulate the beam intensity from 0 to 100% in approximately 0.1 ms. This extremely fast modulation is the fundamental prerequisite for *continuous line scanning*, allowing the dose to be continuously "painted" while the beam moves at maximum velocity without being interrupted.

- **Kicker Magnet:** Placed immediately after the cyclotron, it acts as an ultra-fast switch with a $50\ \mu\text{s}$ reaction time. By deflecting the beam into a collimator block, it can turn the irradiation on and off virtually instantaneously, a feature strictly required for traditional *discrete spot scanning*.
- **Degrader:** A system of rapidly moving carbon wedges that enables fast energy changes. A small energy step, corresponding to a 5 mm shift in the proton range in water, can be executed in less than 50 ms. This 5 mm step size represents the typical spacing required to smoothly overlap individual Bragg peaks and create a homogeneous SOBP.

Together, these upstream components operate in perfect synchrony with the gantry hardware to eliminate dead times. This allows the volumetric re-scanning technique that is commissioned at Gantry 2 for moving-target treatments. This approach could be used for treating the whole target within a single breath-hold, which would then be repeated as a sequence of static irradiations to provide repainting, as an alternative to the gating technique (see Section 1.3). To achieve this, several critical technical challenges had to be overcome, as described in [17].

2.5 Gantry 3: The Latest Expansion

The construction of Gantry 3 was undertaken as a scientific collaboration with Varian Medical Systems and integrated into the existing treatment and accelerator facility at PSI. Technically, Gantry 3 offers the same treatment capabilities as Gantry 2 but, with an irradiation field of $30 \times 40\ \text{cm}^2$, goes even beyond that [15].

Gantry 3 (see Figure 22) is a 360° rotating gantry with a total weight of 270 tons and an envelope diameter of 10.5 meters, resulting in the largest machine installed to date at CPT.

Nine primary magnets, which surround the vacuum pipe, steer the protons to the patient as a beam with one-millimeter precision. Gantry 3 also utilizes the active scanning technique to deflect the proton beam with two orthogonal magnets to be able to cover any 3-dimensional tumor shape [18].

Unlike Gantry 2, Gantry 3 is a "downstream scanning" system; the scanning magnets are placed after the final 135° dipole, allowing for a large maximum field size of $30 \times 40\ \text{cm}$. It supports the same therapeutic energy range of 70-230 MeV and achieves energy layer switching times of 200 ms. An on-board integrated imaging system is employed to verify the placement of the patient directly in the treatment position; indeed, Gantry 3 is also equipped with a 360° co-rotating X-ray system that is upgraded to provide Cone Beam CT (CBCT) capabilities.



Figure 22: *The Varian-designed Gantry 3 integrated into the PSI PROSCAN facility.*

2.6 OPTIS: Ocular Melanoma Treatment

OPTIS is the facility dedicated to the treatment of ocular tumors at PSI. It has a fixed horizontal beamline. Instead of moving the beam around the patient, the optimal direction for the beam to enter the patient is achieved by moving and rotating the patient in front of the fixed beam [15].

The treatment of uveal melanomas at PSI began in 1984. Initially, these treatments were carried out using a 72 MeV beam from Injector 1 in the Optis 1 facility. In 2010, the program was transferred to a newly constructed area, Optis 2 (see Figure 23), which was fully integrated into the PROSCAN cyclotron complex. By the end of 2023, over 8,000 patients with eye tumors have been successfully treated at PSI. The results of proton irradiation for these tumors are excellent. In more than 98% of cases, tumor growth was definitively halted or the tumor was eliminated. In over 90% of cases, the affected eye functionality was preserved [19].

A double-scattering process is applied in the OPTIS nozzle to ensure high transport efficiency of the 70 MeV proton beam. A series of 9 thin scatter foils are used to enlarge phase space such that the beam covers the whole tumor laterally in a uniform way. OPTIS can deliver a homogeneous circular field of maximum 35 mm diameter. The Spread-Out Bragg Peak (SOBP) is realized using dedicated modulator wheels. At PSI different modulation wheels are available, each one offering different range modulation. The most appropriate one is chosen based on eye tumor depth. At the end, this field is collimated for each patient using an individually milled copper collimator aperture. The double-scattering feature and the lowest possible energy of 70 MeV achievable allows for superficial eye melanoma treatment within a very short time of ~ 1 min.

The achieved dose distribution is characterized by a steep distal and lateral fall-off. On average, the lateral and distal penumbras are 1.4 mm and 1.5 mm, respectively. OPTIS



Figure 23: *The Optis 2 treatment area dedicated to ocular melanomas.*

allows precise delivery of the requested range ($2\sigma = 0.13$ mm) and dose in the SOBP ($2\sigma = 1.9\%$).

For accurate patient positioning with respect to the treatment beam, the OPTIS area is equipped with two X-ray units aligned with the treatment isocenter, providing orthogonal imaging of the patient's eye. The patient is seated in a treatment chair facing the nozzle, with their head immobilized using an individual mask and bite block. The chair is mounted on a hexapod robot allowing 6-degrees-of-freedom positioning of the patient. The position of the eye (gazing angle) is defined through a fixation light, a small LED lamp that can be placed at any point in the proximity of the nozzle, which the patient must fixate their gaze upon. Intrafractional motion of the patient's eye is monitored using compact surveillance cameras.

3 Pixel Detector

In this chapter, the main characteristics of the pixel detector [20] are introduced. Together with the device structure and the description of the readout system, the main performances and limitations of this detector are explored.

3.1 Detector Structure

The pixel detector is essentially an Ionization Chamber (IC). A schematic view of the device can be seen in Figure 24.

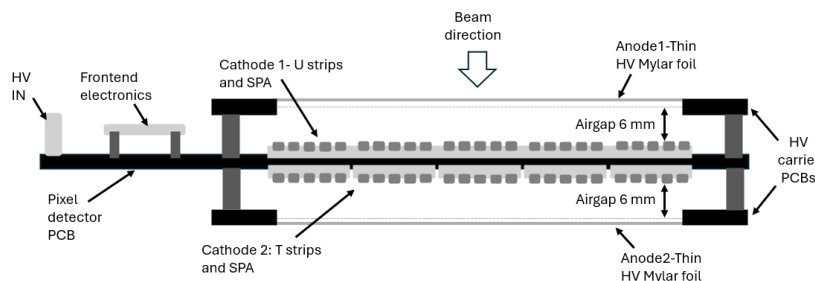


Figure 24: *Pixel detector scheme. Note: the representation is not rigorous.*

The device features two air gaps where particles interact. The use of ambient air as the gas medium results in a very simple and robust design. Ambient air can be used in this kind of detector since we are operating in the ionization regime that implicates that no multiplication of charges occurs. This is possible since the beam intensity is very high and a gain is not necessary. The size of the air gap between the anode and cathode is crucial for signal quality: a larger air gap yields a higher readout signal, but simultaneously decreases the signal rise time. Previous studies identified an optimal gap of 6 mm between the high-voltage (HV) plane and the pixel PCB. The anodes consist of HV planes made of double-metalized 20- μm -thick Mylar foil. Inside the IC, the Printed Circuit Boards (PCBs) are screwed together using spacers. The cathode is represented by the copper structures on the top and bottom of the PCB, while the HV foil itself is glued onto a carrier PCB frame. The detector is operated at 600 V.

The base material used for the PCBs is FR-4, a glass-reinforced epoxy laminate featuring copper on the top and bottom for electrical connections. Current technology allows the manufacturing of PCBs with a stack of 16 layers or more. Hundreds of manufacturers worldwide use this material, guaranteeing a reliable and well-known production process. The PCB design used for our detectors is a multilayer stack with the detector cathodes located on the outer layers. Inside the stack, several copper layers are dedicated either to shielding or to signal routing. The total thickness of the PCB is 1.628 mm. The basic layer stack is shown in Figure 25.

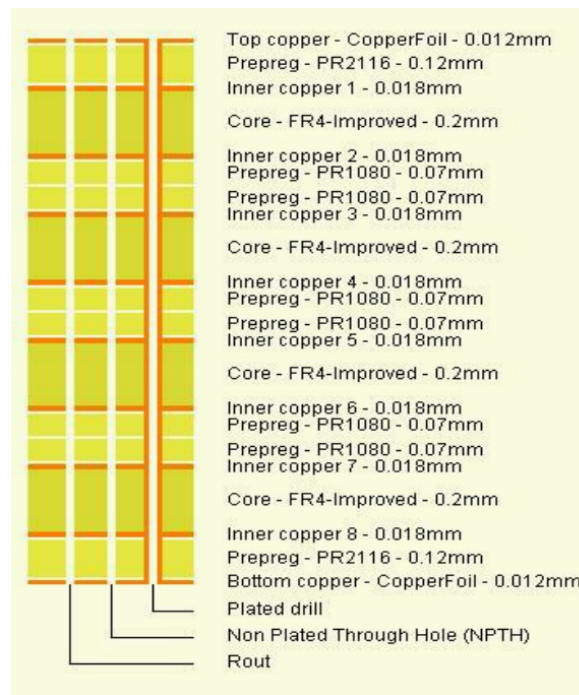


Figure 25: Detailed view of the PCB stack.

At the top of the PCB, a strip-segmented layer is implemented alongside a pixel array built on top of it. An identical structure is present at the bottom of the PCB. The strip orientation at the top is orthogonal to the one at the bottom: in total, there are 7 U-oriented and 5 T-oriented strips. The total signal collected by the detector is the sum of the two pixel layers, which significantly improves the Signal-To-Noise Ratio (SNR). Since the active scanning area of Gantry 2 is 12 cm $\times$ 20 cm, this sets a strict requirement for the detector size. The main building block of the device is an 15 $\times$ 15 small pixel array (SPA), shown in Figure 26.

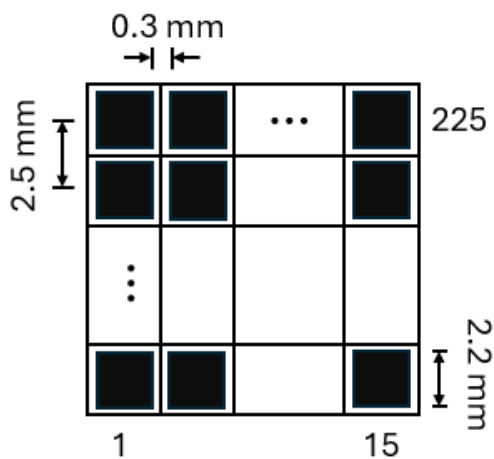


Figure 26: Representation of the Small Pixel Array (SPA).

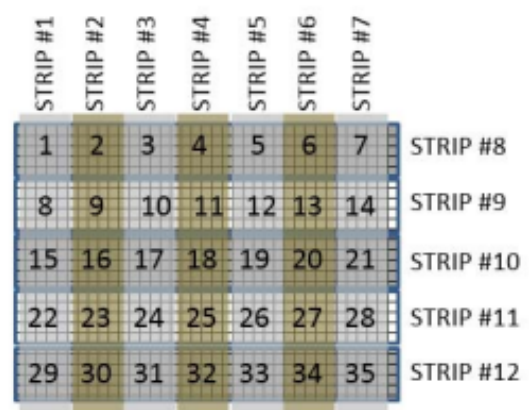


Figure 27: 2D map of the pixel detector active area formed by the intersection of orthogonal strips.

The pixel layers are composed of these SPAs, each containing 15^2 pixels. The overall size

of an SPA must be larger than the largest beam spot, plus a safety margin (the reason for this is explained in the next section). In the current design, each SPA consists of 225 small pixels, and the size of each pixel is $2.2 \text{ mm} \times 2.2 \text{ mm}$. The spacing between adjacent pixels is $300 \text{ }\mu\text{m}$, resulting in an overall pixel pitch of 2.5 mm . Furthermore, the size of the SPA perfectly matches the width of the strips.

In total, the detector comprises a 7×5 matrix of SPAs. To distinguish signals coming from different SPAs, the information from the 12 strips is utilized. Indeed, the superposition of the 12 strips defines exactly 35 large areas, each corresponding to a single SPA (as shown in Figure 27).

3.2 Channel Recycling Technique and Limitations

The resolution of the measurements strictly depend on the pixel size. By decreasing the pixel size, the overall number of required pixels increases, as the number of readout channels required. In addition to the design challenges, the signal measured by smaller pixels decreases proportionally, reducing the SNR and leading to poorer measurement quality.

A further limiting factor is the number of available readout channels. For this pixel detector, a maximum of 256 channels is allowed. The number is defined by the Therapy Control System (TCS). Under this constraint, developing a detector with thousands of pixels represents a major challenge for the PCB layout. The solution implemented is the so-called *Channel Recycling Technique*, illustrated in Figure 28.

Several SPAs cover the active area of the detector, and the individual pixels occupying the same relative position in all SPAs are electrically connected to each other. Each group of connected pixels is then fed into a single readout channel. In this way, every pixel is connected to a channel, but one channel serves multiple pixels simultaneously. Thanks to this method, provided the beam spot is smaller than a single SPA, it generates a signal in only one of the pixels connected to a given readout channel. Moreover, the use of orthogonal strips allows the identification of 35 large areas using just 12 channels.

The detector readout is performed in two steps:

1. The signal information from the strips is used to calculate the raw beam position. This technique works efficiently even if the beam hits several strips simultaneously.
2. The raw position is then used to locate the specific SPA hit by the beam. The detailed 2D profile is subsequently reconstructed from the signals measured by that corresponding SPA.

A critical issue arises if the spot size exceeds the width of a single SPA. In this scenario, the profile reconstruction algorithm fails. The detector still reads all 7875 pixels but, due to the channel recycling technique, the signals collected outside the central SPA are

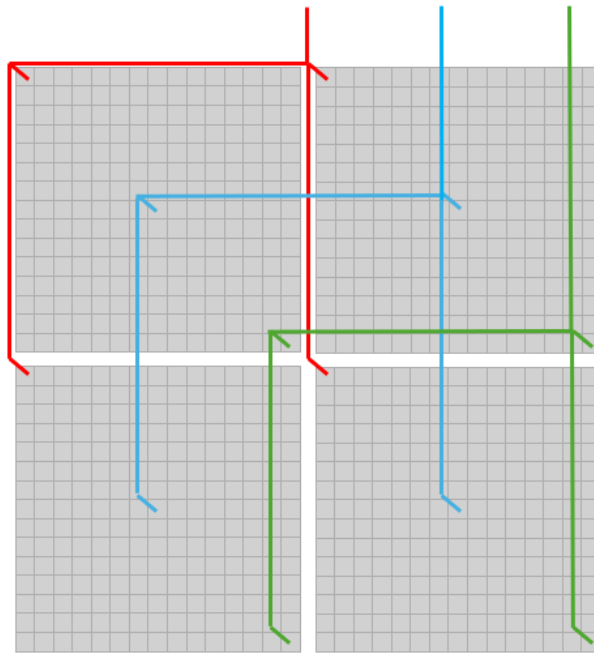


Figure 28: *Illustration of the Channel Recycling Technique working principle. Lines of the same color represent the same readout channel.*

"folded back" and superimposed onto the 225 pixels forming a single SPA, leading to a severe distortion of the actual profile shape. The investigation of this limitation and its implications for clinical dosimetry is the main subject of this research project.

3.3 Detector Readout

The front-end readout electronics must process very small currents, ranging from 10^{-15} to 10^{-9} A, at high acquisition rates. The SPA must be at least as large as the biggest beam spot, plus a safety margin. Moreover, the readout time must deal with a maximum scanning speed of 2 cm/ms [20] since Gantry 2 is optimize for line scanning, even if it was not used with this detector.

These stringent requirements are met by a commercial readout chip: the ADAS1128 [9] from Analog Devices. It is a highly integrated current-to-digital converter featuring 128 input channels, providing integrated current measurements at 24 bit. A digital configuration interface provides the flexibility to remotely adapt the measurement range and readout cycle time, as well as to calibrate the analog portion of the chip. Based on this component, a multichannel current sensor (MCCS) board was developed, featuring an analog interface to the detector and a digital interface to a Field Programmable Gate Array (FPGA) processing system. In addition to reading out the chip, the MCCS board handles power supply distribution, voltage supervision, and ambient temperature measurements. The fully assembled system is shown in Figure 29.



Figure 29: *Picture of the two MCCS boards equipped with the ADAS1128 chips.*

To connect all signals coming from the detector, two readout boards are required (see Section 3.2 for details). The MCCS boards are directly connected via cables to the FPGA readout processing platform.

The core of this platform is an Enclustra module [10] equipped with a Xilinx Kintex-7 FPGA. The module acts as a complete system, including Double Data Rate (DDR) SRAM, flash memory, complex power distribution, and a flexible user I/O interface. The integration of this commercial FPGA module significantly reduced the hardware development time and associated risks. The custom development was limited to a simple carrier board featuring two digital interfaces for the MCCS boards and high-speed optical communication lines connected to the PSI Proton Therapy Control System (TCS).

The FPGA firmware running on the Enclustra board is written in VHDL (Very High Speed Integrated Circuit Hardware Description Language) and features two main interfaces:

1. *Control System Interface:* The TCS is connected to the FPGA via a serial high-speed optical link capable of data transfer rates up to 2 Gbit/s. Data access within the FPGA is managed through internal registers and dual-port memory blocks. Register access is typically used for system configuration and simple telemetry (e.g., temperature and voltage supervision). Dual-port RAMs are used to exchange the massive amount of pixel readout data. One memory block stores the integrated data for each channel, while a second one stores single-sample logging data (up to 512 consecutive samples per channel). This deep integration with the control system ensures that the detector readout cycle is perfectly synchronized with the beam delivery.
2. *MCCS Board Interface:* Communication with the ADAS1134 chips is handled via multiple protocols. A four-wire Serial Peripheral Interface (SPI) configures the measurement range, sets the readout cycle time, and triggers the automatic gain and offset calibration for all 128 channels. For the actual data readout, the chip utilizes a 125-MHz Low Voltage Differential Signaling (LVDS) serial interface. While the hardware allows the readout cycle to be flexibly configured between approximately $50\ \mu\text{s}$ (the theoretical minimum conversion time) and $900\ \mu\text{s}$, the system is operated at 5 kSPS. This results in an effective integration time of $200\ \mu\text{s}$ per sample, providing an optimal balance between high temporal resolution and manageable data transmission limits. Additionally, an I2C system monitor on the MCCS board allows telemetry measurements, accessible by the TCS through the internal FPGA registers.

During standard operation, the detector readout cycle is initiated by a start command from the control system. From the beginning to the end of a single spot, line, or contour delivery, the FPGA reads all channels in a continuous $200\ \mu\text{s}$ loop, integrating the signals until a stop command is received. Simultaneously, all 256 channels are continuously logged. Given the hardware limit of 512 samples per channel and a cycle time of $200\ \mu\text{s}$, the maximum continuous logging duration is 102.4 ms.

After the delivery of a spot-scanning plan, the control system retrieves the integrated signals from all channels. It then calculates the beam position from the large strips and the precise beam width from the 2D profiles measured by the SPAs. This tight coupling between the electronics and the TCS allows the user to monitor each individual spot directly via a Graphical User Interface (GUI) immediately after delivery. A comprehensive scheme of the complete readout chain is shown in Figure 30.

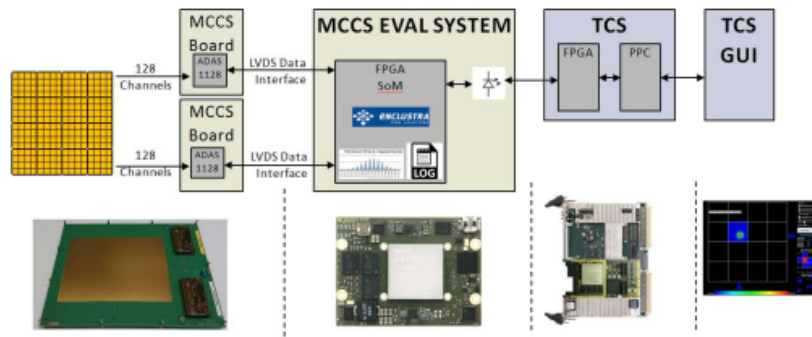


Figure 30: *Schematic representation of the data readout chain.*

The read and storage processes for the continuously logged data are strictly synchronized with the beam delivery. The offline analysis of these logging data is subsequently handled using a dedicated MATLAB application (see Section 4.1.7).

3.3.1 PT Correction

To improve the reliability of the measurements compared to previous studies, additional environmental parameters were acquired: the pressure and temperature of the ambient air inside the active volume of the device. As explained in detail later (see Section 5.3.1), gas pressure and temperature play a fundamental role in the absolute response of unsealed ionization chambers to radiation.

This continuous monitoring was made possible by a Pressure and Temperature (PT) sensor inserted into a dedicated cavity machined into the detector's containment chamber (see Figure 31).

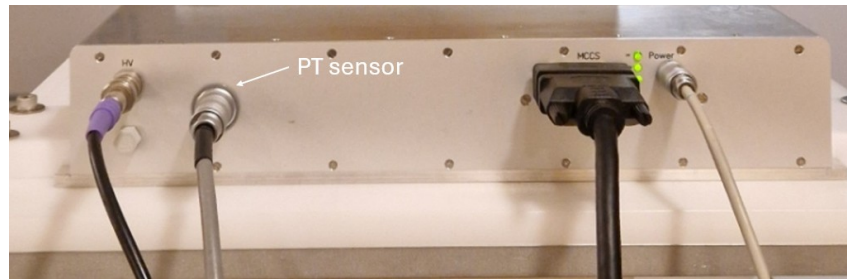


Figure 31: *Profile of the pixel detector containment chamber with a focus on the PT sensor cavity and its connection cable.*

The sensor is a commercial Pt100 probe provided by Günther GmbH Temperaturmesstechnik [21]. The telemetry can be read out and accessed directly from the control room monitors. The absolute pressure (in mbar) and temperature (in °C) are displayed live via a graphical interface. During each field delivery, these values were recorded to be applied as correction factors during the data analysis phase.

4 Data Acquisition

This chapter focuses on the main techniques used to obtain the data. First, the experimental procedures followed for data acquisition with the pixel detector and other reference devices are described. Then, an overview of the TOPAS software and the implemented simulations is given. All data-taking campaigns were performed at Gantry 2 at the Center For Proton Therapy (CPT).

4.1 Experimental Data with Pixel Detector

4.1.1 Single Spots

For the delivery of the single spots, the gantry angle was fixed at 0 degrees, and the spots were delivered at the center of the pixel detector. For this measurement, as well as for all the subsequent ones, the pixel detector was positioned at the isocenter. To study the different parameters linked to the spots, such as the beam size, four different configurations were tested using different nozzle extractions and alternating the automated insertion of a pre-absorber in the nozzle. These configurations are the following:

1. Nozzle extraction 1 cm (NZ1) without pre-absorber.
2. Nozzle extraction 1 cm (NZ1) with pre-absorber.
3. Nozzle extraction 27 cm (NZ27) without pre-absorber.
4. Nozzle extraction 27 cm (NZ27) with pre-absorber.

For each of these setups, 17 different beam energies were tested, ranging from the lowest energy of 70 MeV to the highest of 230 MeV in 10 MeV steps. To increase the statistical significance, 10 spots were delivered for each energy, resulting in a total of 170 spots per configuration. For each single spot, 10^8 protons were delivered in about ~ 500 ms depending on the energy of the protons since at lower energy the beam intensity is reduced due to the degrader and so the delivery time is increased. The precision on the actual number of protons delivered is very high. As can be seen in Paragraph 4.1.7, the data file provides also the number of MUs delivered that compared with the nominal value required give an indication on the precision of the delivery. The precision on the ADC counts is better than 0.1% for all the energies. Figure 32 shows examples of single spot reconstructions.

4.1.2 Dose Field for Cross-calibration

Another delivered field consisted of a sequence of spots arranged to uniformly cover a 10×10 cm² layer. These fields were primarily used for the dose calibration, as described

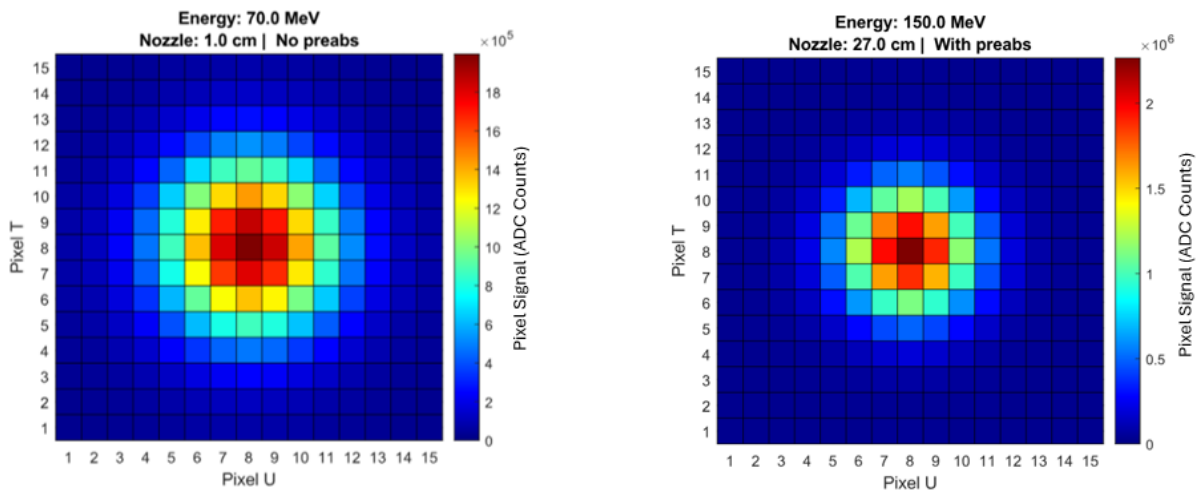


Figure 32: *Single spot reconstruction examples from the pixel detector.*

in Section 5.3. In total, 17 fields were delivered at the center of the pixel detector, one for each energy level (from 70 MeV to 230 MeV, with 10 MeV steps). Each layer is formed by 1681 spots with a regular spacing of 2.5 mm.

The number of protons for the different energies was chosen to deliver the exact same amount of Monitor Units (MUs) for each energy layer. During this acquisition, the nozzle extraction was fixed at 1 cm (NZ1), the gantry position at 0 degrees, and no pre-absorber was inserted. Moreover, to allow a direct comparison with reference dosimetry data, a fixed 1.7 cm slab of PMMA was placed on top of the pixel detector for the entire duration of the acquisition, corresponding to a Water Equivalent Thickness (WET) of about 2 cm. Figure 33 shows examples of these layer reconstructions. (Note: the strict conversion for PMMA thickness should technically be performed using a factor of 1.168 instead of the nominal 1.16).

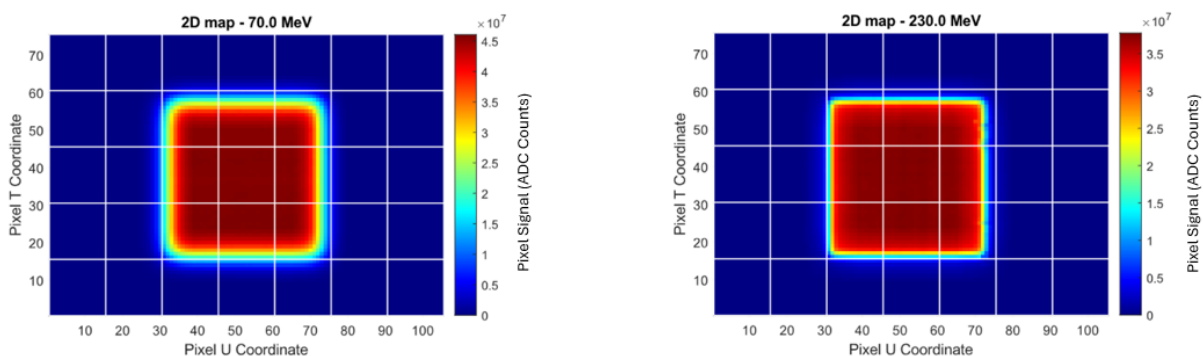


Figure 33: $10 \times 10 \text{ cm}^2$ field reconstruction examples from the pixel detector.

4.1.3 Full Scanning Range Field

Similar to the previous configuration, larger uniform fields were delivered over the active area of the pixel detector; these were also utilized for the dose calibration studies (see

Section 5.3.2). The dimensions of these fields are $20 \times 12 \text{ cm}^2$. One field was delivered for each energy, this time ranging from 70 MeV to 230 MeV with finer 5 MeV steps.

Each layer is formed by 1025 spots with a spacing of 5 mm. As before, the number of protons was adjusted to deliver a constant amount of MUs across all energy layers. The nozzle extraction remained at 1 cm (NZ1), the gantry at 0 degrees, and the pre-absorber was removed. A 1.7 cm PMMA slab was kept on top of the detector. Figure 34 displays reconstructions of these larger layers.

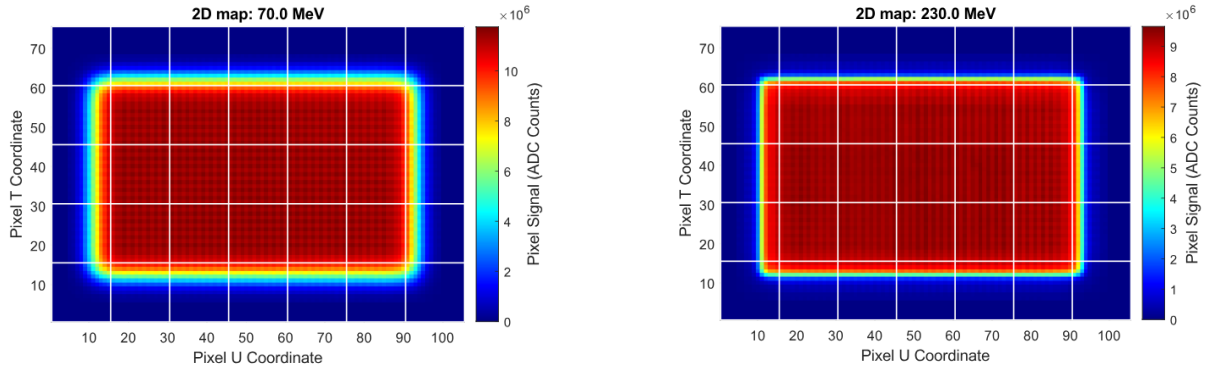


Figure 34: $20 \times 12 \text{ cm}^2$ field reconstruction examples from the pixel detector.

4.1.4 Dose Box

An important clinical validation was performed using the $6 \times 6 \times 6 \text{ cm}^3$ "Dose Box", a standard field usually utilized for daily Quality Assurance (QA). This specific field is designed to create a Spread-Out Bragg Peak (SOBP) with a uniform dose delivery of 1 Gy in the plateau region. The field consists of the sequential delivery of multiple $6 \times 6 \text{ cm}^2$ layers. To achieve the flat SOBP, different layers, each one corresponding to a single energy value, are delivered. Different layers have different dose weights (consisting in a different number of protons/MUs delivered). Each layer comprises 289 spots with a spacing of 4.0625 mm. In total, a sequence of 54 layers was delivered, rescanning for each energy slice. During the data acquisition, several depths along the SOBP were investigated by placing different thicknesses of PMMA on top of the Pixel Detector. For all measurements, the nozzle extraction was fixed at 27 cm (NZ27) and the gantry angle at 0 degrees. The acquisitions were performed both with and without the pre-absorber. A summary of the configurations is provided below:

1. 23 mm PMMA, NZ27 with and w/o pre-absorber.
2. 33 mm PMMA, NZ27 with and w/o pre-absorber.
3. 43 mm PMMA, NZ27 with and w/o pre-absorber.
4. 53 mm PMMA, NZ27 with and w/o pre-absorber.
5. 63 mm PMMA, NZ27 with and w/o pre-absorber.

6. 73 mm PMMA, NZ27 with and w/o pre-absorber.

The nominal center of the dose box, corresponding to the center of the SOBP plateau, is located at a depth of 73 mm. Examples of reconstructions for the final layer of the dose box are shown in Figure 35.

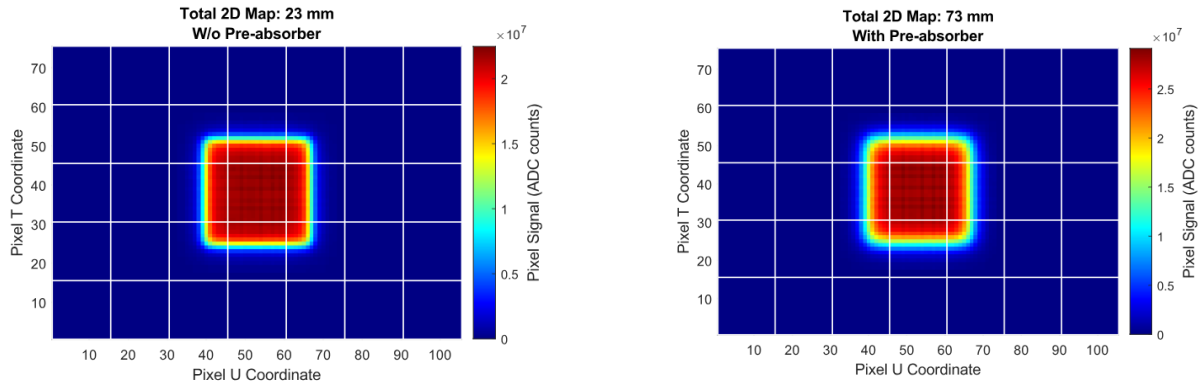


Figure 35: *Dose box final layer reconstruction examples from the pixel detector.*

4.1.5 Patient's Treatment Plans

As a final, stringent validation for the reconstruction and dose calibration algorithms, two clinical fields extracted directly from the Treatment Planning System (TPS) were tested. These fields, labeled F0 and F1, feature highly non-uniform, complex shapes. The required beam energies span from 70 to 120 MeV. The nozzle extraction was fixed at 8 cm and the pre-absorber was not inserted. The fields were investigated at three different depths: 1 cm, 1.4 cm, and 3.9 cm in PMMA. Figure 36 shows the expected dose distributions for F0 and F1 as generated by the TPS at 1 cm depth.

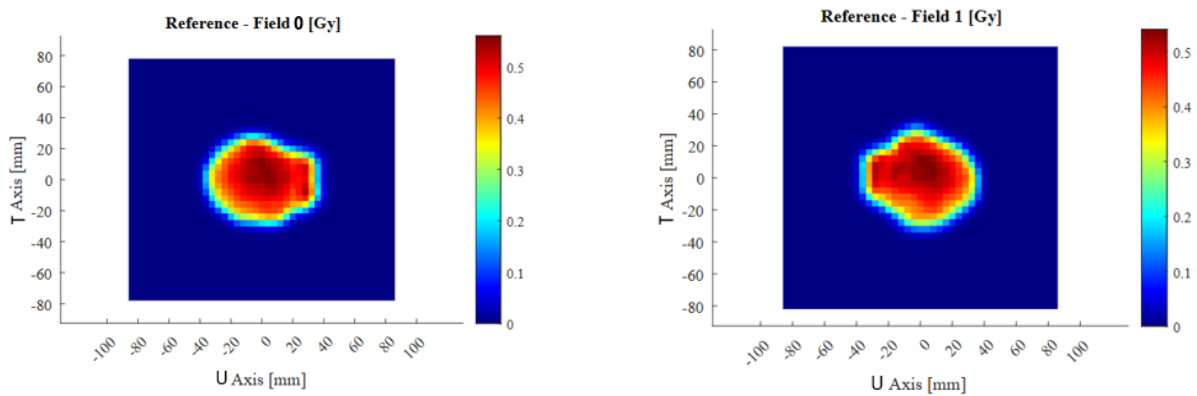


Figure 36: *Patient treatment fields F0 and F1 at 1 cm depth, exported from the TPS.*

4.1.6 Bragg Peak Scan

A dedicated data-taking shift focused on the reconstruction of pristine depth-dose curves (Bragg peak scans). This was performed for 17 different energies (from 70 MeV to 230 MeV in 10 MeV steps). The longitudinal signals were collected by progressively increasing the thickness of PMMA slabs placed on top of the pixel detector.

For each depth, 170 spots were delivered (10 for each energy), maintaining the same parameters used for the single-spot acquisitions (see Section 4.1.1). Each spot consisted of 10^8 protons. The nozzle extraction was fixed at 1 cm without the pre-absorber. Figure 37 illustrates the reconstruction of the depth-dose curves obtained by integrating the signals of the sampled spots.

To achieve a higher longitudinal resolution in the Bragg peak region, an additional dense scan was performed specifically for the 150 MeV beam, sampling many more points around the peak. In this high-resolution measurement, 20,000 MUs were delivered for each spot, instead of relying on the standard 10^8 protons metric.

4.1.7 Data Format and Conversion

The raw experimental data were recorded during beam delivery in the form of binary files (QALog). To make this massive amount of data accessible for numerical analysis, the files were parsed and processed using a dedicated Python script. This script successfully extracted all the relevant machine parameters—such as energy, MUs, nominal and actual spot positions—and matched them with the corresponding Pixel Detector signal matrices. Finally, it converted the output into a standard tabular format ready to be imported into MATLAB.

In this structured format, each row represents the delivery of a single spot. The columns provide telemetry and detector response data. The most critical arrays for the analysis contain the raw machine parameters and the 15×15 pixel matrices (representing the 225 channels of the hit SPA). The table also logs the gantry angle, nozzle extraction, pre-absorber status, and pulse duration.

Furthermore, the Python script automatically performs a 2D Gaussian fit [22] over the raw detector signals. The results of the fit—including the spatial standard deviations σ_x and σ_y , the geometrical offsets, and the peak amplitude—are appended to the table. Combining all these parameters makes it straightforward to geometrically reconstruct the exact position and shape of each single spot on the active surface of the pixel detector.

By knowing the absolute spatial coordinates of the hit SPAs, complex fields generated by thousands of spots can be effortlessly reconstructed by superimposing and summing the signals of each individual pixel matrix according to their reciprocal relative positions.

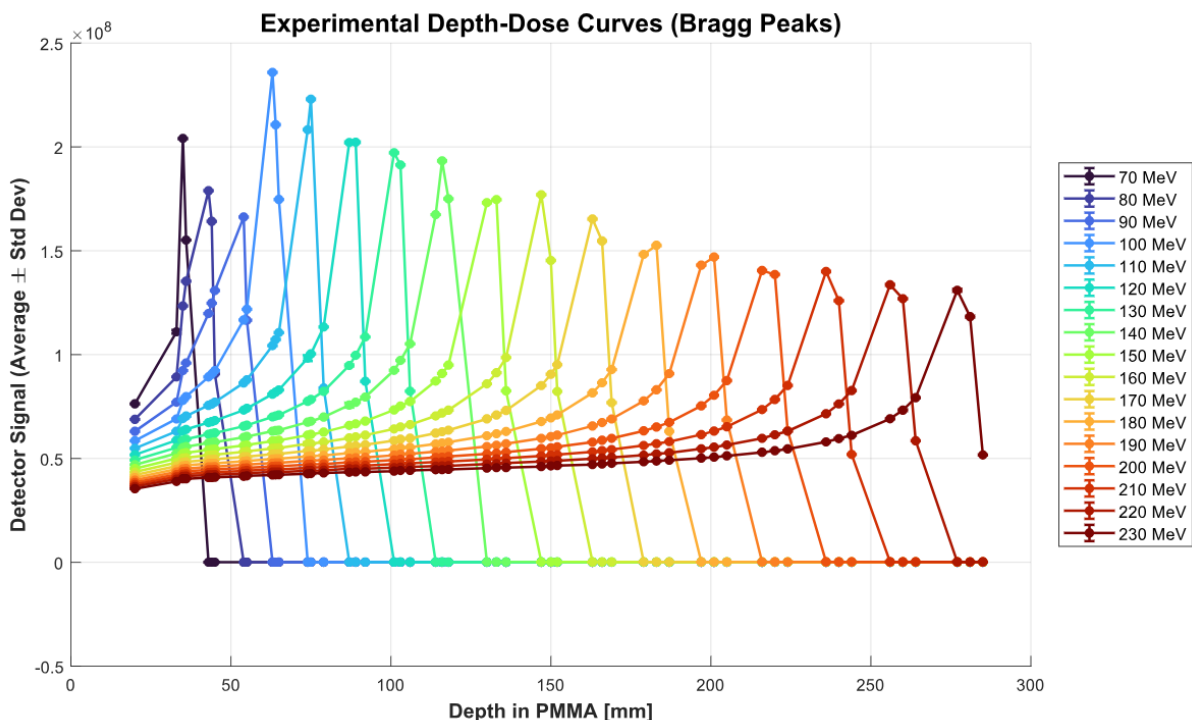


Figure 37: *Depth-dose pristine curves reconstructed from the pixel detector data.*

4.2 Experimental Data with CMOS Camera and Range Scanner

To validate the experimental data acquired with the pixel detector, independent measurements were performed using reference devices. In this section, the CMOS Camera and the Range Scanner are briefly introduced, along with the main data-taking campaigns conducted to acquire the ground-truth benchmark data.

4.2.1 CMOS Detector

The architecture of this detector is straightforward. It essentially consists of a scintillating screen coupled to a Complementary Metal-Oxide-Semiconductor (CMOS) Camera. A picture of the device is shown in Figure 38.

The scintillating screen is a commercially available $\text{Gd}_2\text{O}_2\text{S:Tb}$ (P43) inorganic phosphor foil (CAWO Solutions, Schrobenehausen, Germany). P43 is one of the most widely adopted scintillators for radiobiological and dosimetric applications, featuring a characteristic emission peak at 545 nm. The exposed active area of the foil is approximately $258 \times 238 \text{ mm}^2$. The optical photons produced by the proton beam interactions are deflected by a 45° -tilted mirror and routed through a lens system into the CMOS sensor. The sensor is a QHY128c Pro (QHYCCD, Beijing, China), a high-end camera designed for deep-sky astrophotography [23], offering extremely low thermal noise.

The CMOS detector was used for two primary measurements. The first campaign focused



Figure 38: *The CMOS detector installed at Gantry 2 at PSI.*

on the acquisition of single beam spots. Two specific configurations were tested:

1. Nozzle extraction 1 cm (NZ1) without pre-absorber.
2. Nozzle extraction 27 cm (NZ27) with pre-absorber.

For each configuration, 10 spots for each energy slice (from 70 MeV to 230 MeV in 10 MeV steps) were delivered, with 10^7 protons per spot. To increase the signal-to-noise ratio, the final reference image is the mathematical integration of the 10 spots. Additionally, a "dark frame" acquisition (without beam delivery) was systematically performed to estimate and subtract the optical and thermal background noise.

The second measurement aimed to validate the Dose Box field. The procedure closely mirrored the one used for the pixel detector. The exact same complex field was delivered, but six different PMMA thicknesses were placed directly on top of the scintillating foil. Due to the intrinsic design of the CMOS casing—which inherently features a 4 mm PMMA slab above the screen—this extra material budget had to be carefully accounted for when calculating the total depth. The tested configurations were:

1. 19 mm PMMA, NZ1 with and w/o pre-absorber.
2. 29 mm PMMA, NZ1 with and w/o pre-absorber.
3. 39 mm PMMA, NZ1 with and w/o pre-absorber.
4. 49 mm PMMA, NZ1 with and w/o pre-absorber.
5. 59 mm PMMA, NZ1 with and w/o pre-absorber.
6. 69 mm PMMA, NZ1 with and w/o pre-absorber.

It is important to note the forced choice of the 1 cm nozzle extraction for these runs. Due to strict physical space limitations in the treatment room, stacking thick PMMA slabs on top of the bulky CMOS chassis does not allow for a full 27 cm nozzle extraction without causing mechanical collisions. Dark frames were also acquired for these measurements to ensure rigorous background subtraction.

4.2.2 Range Scanner

The Range Scanner (RSC) is the gold-standard electromechanical system used to perform Integral Depth Dose (IDD) or high-precision point-dose measurements in water across all Gantries at CPT.

The system consists of a PMMA water tank equipped with two interchangeable entrance windows: a round window (2 mm thick) and a rectangular window (5 mm thick). To switch between the windows, the entire tank assembly can be mechanically rotated by 180°. The core of the RSC is a high-precision motorized stage used to drive a field Ionization Chamber (IC) longitudinally through the water. A picture of the Range Scanner is provided in Figure 39.

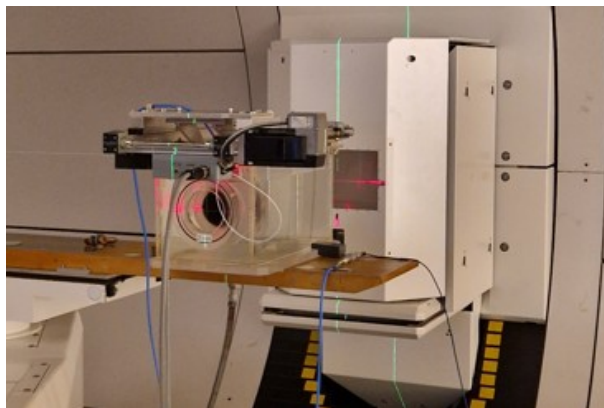


Figure 39: *The Range Scanner (water phantom) positioned at Gantry 2 at PSI.*

To read the IC signals, the system relies on an external electrometer, a Current-to-Frequency-Converter (CFC), and dedicated HV sources. The tank also houses a built-in PT-100 probe for real-time water temperature monitoring. The entire drive and readout chain is controlled by custom software developed in the LabVIEW environment. The IC can be continuously moved over an impressive range of 1 to 450 mm. The round entrance window has a diameter of 100 mm and a strict WET of 2.338 mm, whereas the square window offers a lateral clearance of 210 mm and a WET of 5.85 mm.

The Range Scanner provided reference data used for absolute comparisons with the pixel detector. Most importantly, it was used to establish the absolute reference dose delivered at a 2 cm depth (WET) by pristine beams of varying energies (from 70 MeV to 230 MeV in 10 MeV steps). During those historical acquisitions, pressure and temperature logs were also strictly recorded.

Furthermore, the RSC provided the high-resolution IDD benchmark curves used to validate the Bragg peak scans. Thanks to its motorized stage, the Range Scanner can collect hundreds of data points along the longitudinal axis, resulting in the most precise spatial reconstruction of the Bragg peak available and serving as the ultimate tool for beam range verification.

4.3 Simulations with TOPAS

Monte Carlo simulations play a fundamental role in the data analysis pipeline. Comparing simulated models with experimental data allows researchers to assess the reliability of the detector’s geometric response and the validity of the applied calibration factors.

In this project, the TOPAS (TOol for PArticle Simulation) platform was used [24]. TOPAS is a dedicated, user-friendly extension of the powerful Geant4 Simulation Toolkit [25], specifically designed to simplify the complex physics simulations required by medical physicists in radiotherapy applications.

The methodologies used to model the clinical environment and the simulation logic are detailed below.

4.3.1 Simulation of Beam Source, Pixel Detector and Experimental Setup

To properly simulate the different treatment fields, accurate beam models are mandatory. For this project, validated reference beam models for Gantry 2—previously developed by other researchers at PSI—were utilized. These phase-space files contain precise parametric descriptions of the beam energy, energy spread, and transverse spot sizes (σ_x, σ_y) at the nozzle exit. Specific models are available for different energies and all permissible nozzle extractions. These files also define the geometric origin of the source relative to the machine isocenter.

Starting from these models, only a few additional geometric volumes were needed to replicate the experimental setups. Firstly, PMMA slabs of varying thicknesses were generated and placed in front of the detector to simulate different measurement depths. In TOPAS, this is achieved straightforwardly by defining the geometric boundaries and assigning the correct material properties.

Similarly, the pre-absorber was modeled. For simplicity and computational efficiency, the graphite pre-absorber was simulated as a block of pure water with a thickness of 4.2 cm, exactly matching the WET of the real physical component. The critical aspect of modeling the pre-absorber is its longitudinal positioning, which must dynamically adapt to the nominal nozzle extraction. Since the simulated proton source is always fixed at the theoretical nozzle exit plane, the pre-absorber volume must be positioned immediately downstream of that specific coordinate (e.g., at 27 cm from the isocenter for an NZ27 setup, or at 1 cm for an NZ1 setup).

The final crucial element is the geometric modeling of the pixel detector itself. Replicating the exact microscopic structure of the real device is highly inefficient, as it would require modeling four distinct, extremely thin scoring layers (two for strips, two for pixels) alongside all the complex PCB material budget sandwiched between them. A simplified, computationally efficient approach was initially adopted. The entire detector was simulated using homogeneous water, translating the physical thickness of all solid components into their WET equivalents. A single virtual scoring layer was defined and placed behind a water slab whose thickness equaled exactly half of the total WET of the real PCB stack. This physical approximation effectively simulates an "average" response between the top and bottom physical pixel layers.

In Section 4.4, the dosimetric implications of this simplified geometry versus more complex designs are quantitatively discussed. Unless otherwise specified, this "single-layer" water-equivalent model was the standard geometry used for all simulations presented hereafter.

4.3.2 Simulation of Single Spots

The simplest simulated scenario involves single static spots. Using a custom Bash script, it was possible to fully automate the generation and execution of the TOPAS parameter files. The script iteratively parses the required input variables: nozzle position, pre-absorber status, number of simulated protons per spot, and total number of spots per energy slice.

The goal was to generate synthetic datasets directly comparable with the experimental ones described in Section 4.1.1. For each energy, 10 independent spots were simulated, each containing 100,000 primary particles (protons). The four standard configurations were tested:

1. Nozzle extraction 1 cm (NZ1) without pre-absorber.
2. Nozzle extraction 1 cm (NZ1) with pre-absorber.
3. Nozzle extraction 27 cm (NZ27) without pre-absorber.
4. Nozzle extraction 27 cm (NZ27) with pre-absorber.

It is crucial to note that the theoretical beam models provided in the library did not perfectly match the exact energies delivered experimentally. Since the primary goal of this specific simulation was to analyze the transverse spot size (and its widening) relative to the pixel detector and CMOS responses, the script automatically selected the available beam model with the energy closest to the real one. This same approximation was accepted for the Bragg peak scans (see Section 4.3.4), whereas for the Dose Box simulations, the experimental energies matched the available models perfectly. Figure 40 shows the 2D energy deposition of simulated single spots.

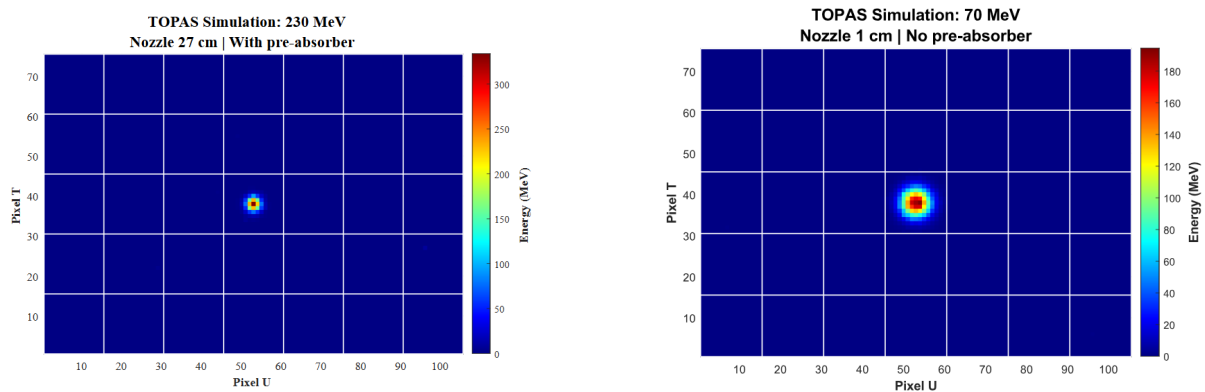


Figure 40: *2D energy deposition maps of simulated single spots using TOPAS.*

4.3.3 Simulation of Dose Box

Simulating the Dose Box required a significantly more complex automation script. The main challenge arises because the final dose layer is the superposition of multiple energy slices, and each energy slice requires a highly specific, heavily modulated number of protons. Furthermore, each energy layer is not a static spot, but a dynamically scanned 6×6 cm² field.

To orchestrate this, a pre-processing MATLAB script was developed. This script performs two distinct tasks. First, it parses the experimental machine log files to extract the exact sequence of delivered energies and the precise spatial coordinates (x, y) of every single spot composing the macroscopic field. These arrays are then formatted into TOPAS syntax to dictate the beam model selection and the dynamic beam steering.

The second, more complex task is translating the clinical MUs into a simulated number of protons. As explained in Section 4.1.7, the machine logs only record the delivered MUs, which have a non-linear, highly energy-dependent relationship with the actual number of physical protons. To solve this, seven empirical calibration curves (extracted from clinical QA data) were utilized, showing the MU-to-proton relationship at 5×10^5 , 10^6 , 5×10^6 , 10^7 , 3×10^7 , 6×10^7 , and 10^8 protons. The script interpolates these curves: for every layer, it takes the logged MUs and the nominal energy, and computes the exact physical number of protons delivered.

Because simulating billions of protons for a single Dose Box would require unfeasible computational clusters, a global scaling factor was applied. The script assigns a normalized statistical weight to each energy layer, drastically reducing the absolute number of simulated histories while strictly preserving the clinical proportionality between different energies. The output is a massive TOPAS parameter file.

The TOPAS engine reads this steering file and sequentially simulates the spots to generate the integrated field. This entire process was repeated for the six different PMMA depths investigated experimentally. An example of the simulated dose deposition for the final layer is shown in Figure 41.

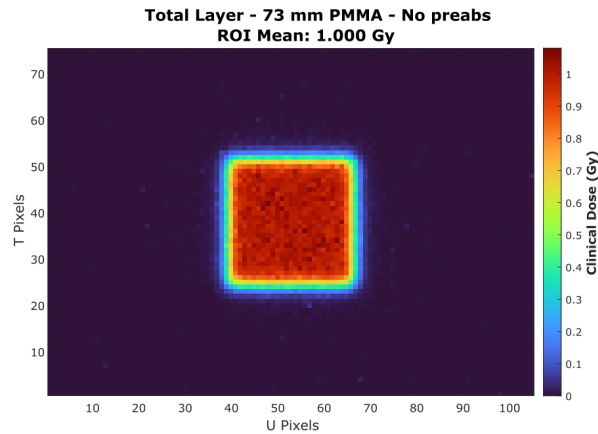


Figure 41: *Example of the integrated energy deposition for the simulated final layer of the Dose Box.*

4.3.4 Simulation of Bragg Peak

The Bragg peak simulation utilized the same logic as the single spots. For a given depth, one static spot was generated for each of the 17 energies, using 10,000 protons per spot. The bash script was configured to iteratively increase the thickness of the PMMA slab in front of the detector, spanning the same longitudinal range investigated experimentally. The nozzle was fixed at 1 cm without a pre-absorber.

Figure 42 displays the simulated depth-dose curves. As previously mentioned, these specific curves cannot be used for absolute point-to-point comparison with the experimental data due to the slight mismatch between the experimental energies and the available theoretical beam models. Nevertheless, this simulation was fundamental to verify the geometric integrity of the simulated environment, ensuring that the physical scaling laws and the longitudinal energy deposition matched the theoretical expectations.

4.4 Considerations about Different Detector Design

As detailed above, the baseline geometry of the pixel detector in TOPAS was highly simplified: a single scoring layer positioned at the mid-plane of a water-equivalent PCB slab. To evaluate how much this geometric approximation influences the dosimetric results, alternative simulation models were implemented and compared.

The sensitivity study was performed on single spots. The simulation framework described in Section 4.3.2 was executed using two new detector topologies. The first model completely removed the upstream PCB slab, placing the active scoring layer immediately at the air-detector interface (see Figure 43a). This geometry mimics the physical response of the top-most pixel layer of the real detector. The second model placed the scoring layer behind a water-equivalent slab twice as thick as the reference one (see Figure 43c), mimicking the response of the bottom-most pixel layer buried under the entire PCB stack. (The complex double-layer design shown in Figure 43d will be discussed in Section 5.7).

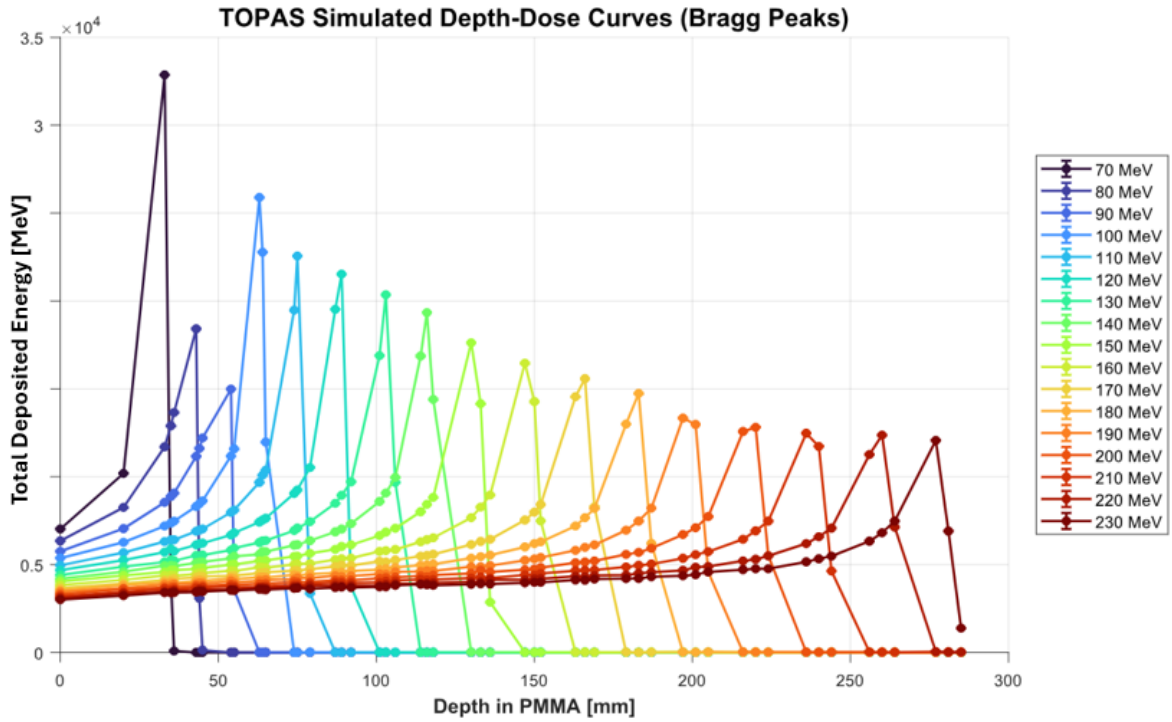


Figure 42: *Simulated depth-dose pristine curves generated with TOPAS.*

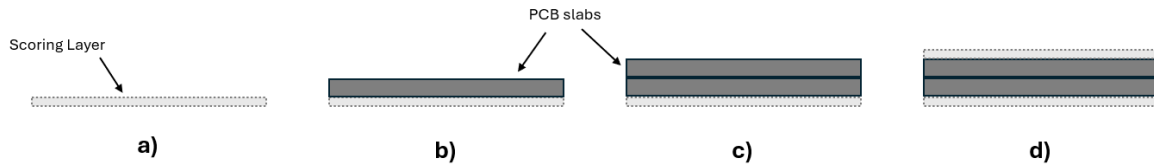


Figure 43: *Schematic representation of the different pixel detector geometries modeled in TOPAS.*

For both new topologies, 10 spots for each of the 17 energies were simulated (100,000 protons per spot). To limit computational time, only two extreme configurations were tested:

1. Nozzle extraction 27 cm (NZ27) with pre-absorber (high scattering).
2. Nozzle extraction 1 cm (NZ1) without pre-absorber (low scattering).

A MATLAB script analyzed the simulated output matrices, fitting a 2D Gaussian to extract the mean peak signal and the Full Width at 10% of Maximum (FW10M) for each spot. The percentage difference between these new values and the ones obtained with the reference mid-plane geometry (Figure 43b) was calculated. The mean signal provides information on the absolute energy deposition (dosimetry), while the FW10M tracks the spatial widening of the spot due to internal scattering. The results are summarized in Table 1.

Energy (MeV)	NoBulk vs Ref		DoubleBulk vs Ref	
	Δ Signal (%)	Δ FW10M (%)	Δ Signal (%)	Δ FW10M (%)
80	-8.13	+0.21	+12.62	-0.13
90	-3.12	+0.63	+4.30	-0.25
100	-2.26	+0.16	+2.55	-0.03
110	-1.54	+0.71	+1.99	+0.35
120	-1.83	+0.82	+1.16	+0.62
130	-1.73	+0.63	+1.49	+0.06
140	-1.96	+0.13	+1.05	-0.12
150	-2.35	-0.22	+0.46	-0.40
160	-2.02	-0.06	+0.66	-0.17
170	-1.98	+0.04	+0.80	-0.14
180	-2.03	-0.41	+1.44	-0.81
190	-2.81	+0.54	+1.05	+0.72
200	-3.31	-0.93	+1.04	-0.44
210	-3.07	+0.06	+0.78	+0.64
220	-2.93	+0.96	+0.96	+1.14
230	-3.73	+0.20	+0.86	+0.39

(a) Configuration: NZ27 With Pre-absorber

Energy (MeV)	NoBulk vs Ref		DoubleBulk vs Ref	
	Δ Signal (%)	Δ FW10M (%)	Δ Signal (%)	Δ FW10M (%)
70	-2.42	+0.30	+2.29	+0.17
80	-1.67	+0.61	+1.94	-0.01
90	-2.02	+0.41	+1.40	+0.46
100	-1.98	+0.23	+1.73	-0.06
110	-1.75	-0.25	+1.35	-0.05
120	-2.05	+0.26	+1.23	+0.20
130	-1.90	-0.81	+1.08	-1.17
140	-2.53	+0.11	+1.08	+0.53
150	-2.61	-0.18	+1.34	-0.49
160	-3.00	-0.02	+0.80	-0.42
170	-3.11	+0.50	+1.50	+0.87
180	-4.13	-0.54	+0.80	+0.40
190	-4.05	-1.14	+0.83	-1.62
200	-3.91	+0.23	+0.87	+0.65
210	-3.52	-0.65	+0.65	+0.04
220	-3.97	+0.05	+1.35	+0.31
230	-4.20	-0.81	+0.89	+1.89

(b) Configuration: NZ1 No Pre-absorber

Table 1: Percentage differences of peak Signal and FW10M for the NoBulk (fig. 43:a) and DoubleBulk (fig. 43:c) detector geometries compared to the reference mid-plane design (fig. 43:b).

The data clearly demonstrate that for both extremes of nozzle configuration, the variation in the FW10M metric is systematically below 1%, indicating that the macroscopic spatial profile of the spot is relatively immune to the internal material budget of the PCB.

Conversely, the peak signal amplitude shows larger deviations, generally in the order of 2-3%, exhibiting a clear energy dependence. Notably, in the highly scattered configuration (with pre-absorber), low-energy beams show severe deviations (e.g., +12.62% at 80 MeV). This occurs because the internal PCB thickness forces the scoring layer closer to the steep gradient of the Bragg peak region, causing a dramatic surge in energy deposition.

These results prove that the single mid-plane scoring layer is a robust and acceptable approximation for spatial reconstructions, provided the measurements are performed in the plateau region of the depth-dose curve. However, as demonstrated in Section 5.7, in the direct vicinity of the Bragg Peak, this simplified model fails, and the full multi-layer material budget must be rigorously accounted for.

5 Data Analysis

This chapter describes the data analysis procedures and presents the main experimental results. It provides a detailed discussion on the reliability of the pixel detector for clinical dosimetry studies, supported by an extensive comparison with TOPAS Monte Carlo simulations and reference data from other detectors.

5.1 Single Spot Analysis

At the core of the proton pencil beam scanning delivery system is the single spot. For this reason, it is crucial to perform a preliminary study on the single spot reconstruction performed by the pixel detector, focusing on the potential complications arising from the channel recycling technique.

As explained in Chapter 1, to reduce the number of readout channels on the PCB, each pixel is electrically connected to the same channel as all the other pixels occupying the exact same relative position across different SPAs. This clever approach conceals a problematic consequence: if the physical beam spot size is larger than a single SPA, the reconstruction algorithm fails. During beam delivery, the entire active area is read out, but all the signals are ultimately "folded" into a single 15×15 matrix (225 pixels). Any charge deposited outside the central SPA boundary is simply summed back inside, completely distorting the correct spot profile. Therefore, studying the spot size evolution for different energies, pre-absorber setups, and nozzle extractions is fundamental.

Figure 44 shows several 2D profiles of single spots measured with the pixel detector. It is important to note that the spot size decreases for higher energies. Furthermore, the spot becomes significantly broader when the pre-absorber is inserted, and narrower for larger nozzle extractions. All these features are in perfect agreement with the underlying physics of proton scattering in air and matter.

To better visualize how the spot widens at lower energies, the total signal collected exclusively in the outermost perimeter of the SPA can be plotted for all the analyzed configurations (Figure 45).

These plots demonstrate that, especially in configurations with the pre-absorber inserted, the signal at the edges of the pixel matrix increases dramatically. This rising edge signal is a clear indicator that the spot is broadening and eventually becoming larger than the 15×15 matrix. Conversely, in the optimal configuration to minimize spot size (NZ27 without pre-absorber), the signal in the outer border remains consistently low and stable. A similar, yet more indicative, representation can be obtained by plotting the geometric offsets derived from the Python 2D Gaussian fit for each energy across the different configurations (Figure 46).

The general behavior is identical. This occurs because the signal deposited outside the central SPA is artificially folded back inside the matrix by the readout electronics, gen-

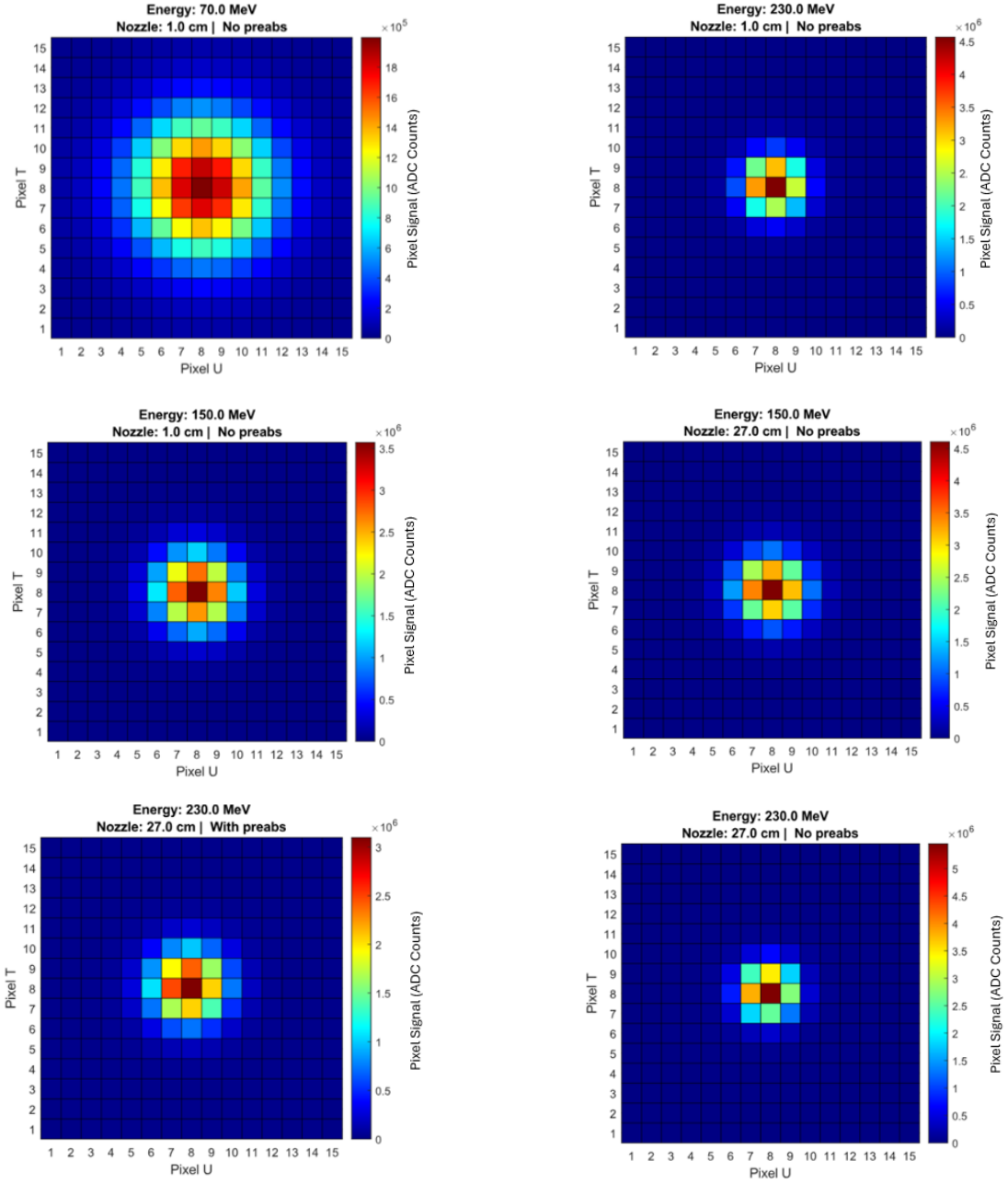


Figure 44: *Single spot reconstructions for different energies and configurations.*

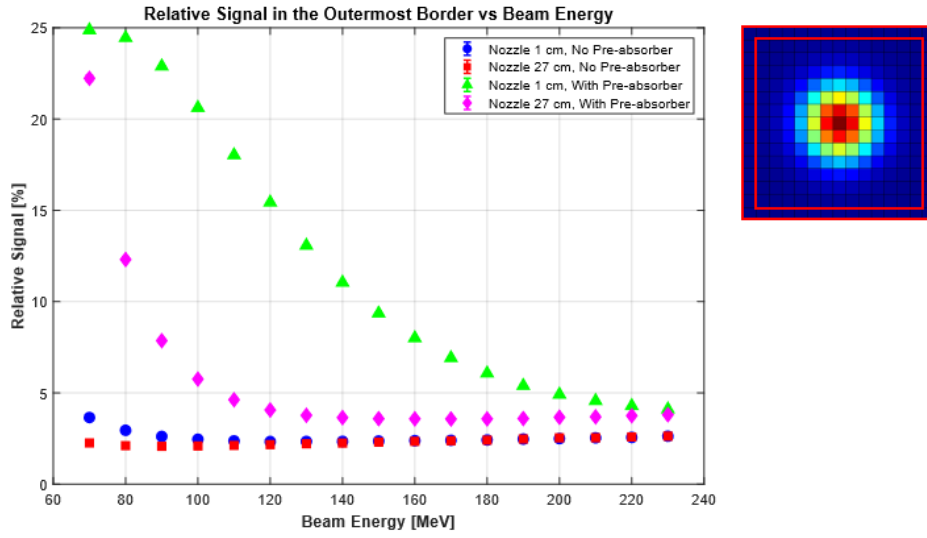


Figure 45: *Relative signal in the outermost border of the SPA for the four different configurations of single spots. Each dot represents the average of 10 spots delivered under the same conditions.*

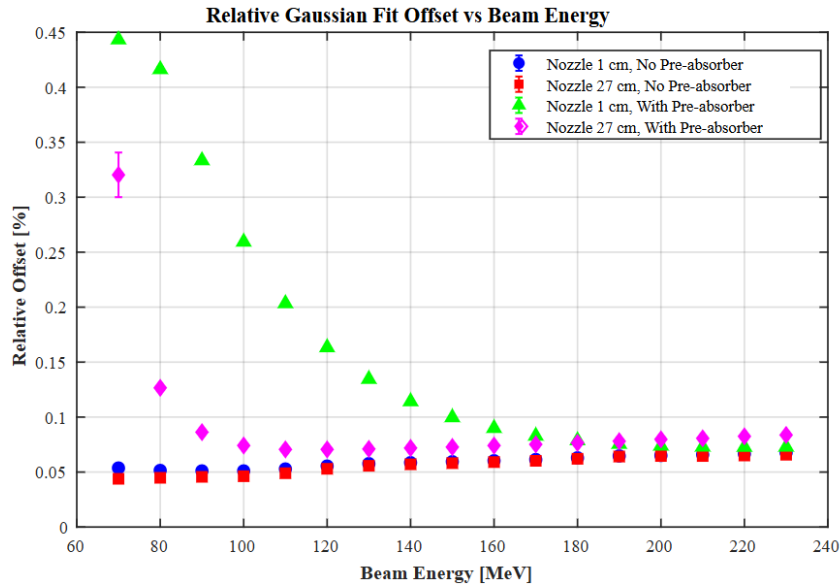


Figure 46: *Relative spatial offset calculated from the Gaussian fit for the four configurations. Each dot is the average of 10 spots.*

erating a general "shift" in the amplitude of the fitted Gaussian tail. To visually clarify this artifact introduced by the channel recycling technique, refer to Figure 47.

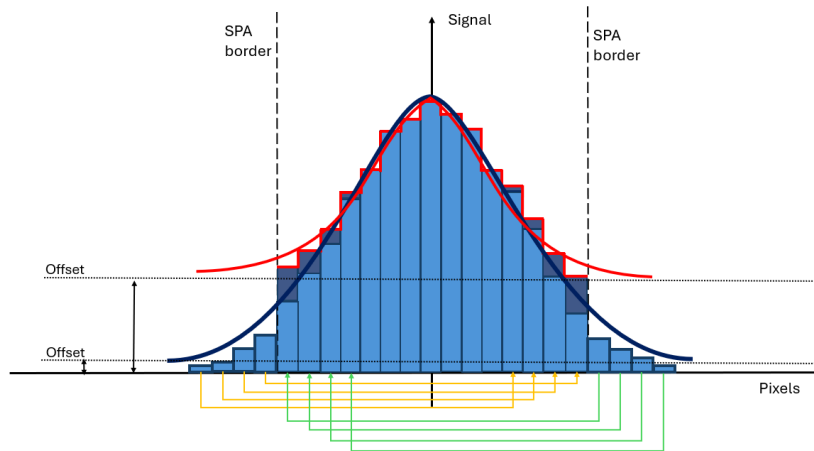


Figure 47: *Schematic illustration of the offset increase effect caused by the channel recycling technique.*

This effect can also be fully appreciated by directly comparing the 2D spot profiles reconstructed by the pixel detector against the true pristine profiles obtained from TOPAS simulations and the CMOS camera. For the latter two, this folding artifact is absent since the signal is collected continuously over the entire scanning area without channel multiplexing limitations. The configurations studied for this direct comparison were NZ27 with pre-absorber and NZ1 without pre-absorber, as these match the specific CMOS data acquisitions (see Section 4.2.1).

Figures 48 and 49 display the direct comparison of the 2D profiles obtained from the different acquisition methods.

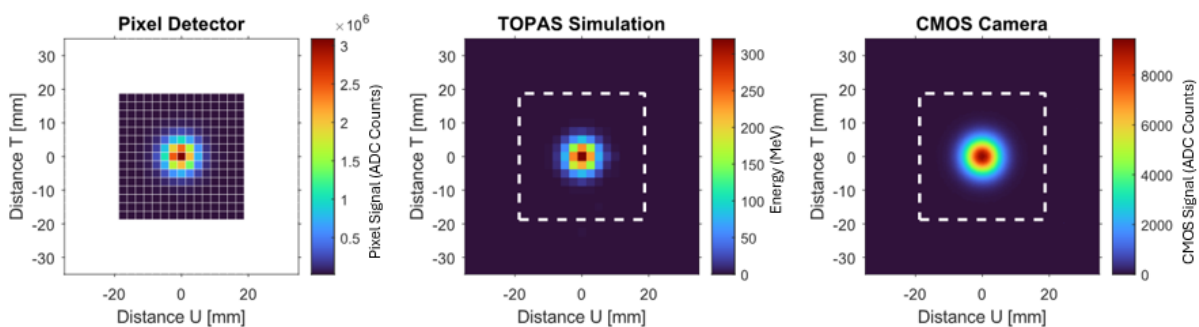


Figure 48: *Comparison of 2D profiles for 230 MeV single spots. The white dashed line represents the physical size of a single SPA.*

It is evident that for 230 MeV beams, the spot is highly focused and completely contained within the SPA boundaries (represented by the white dashed box). Consequently, all three profiles look nearly identical. The situation changes drastically for 80 MeV spots. Here, a significant halo is visible extending outside the SPA border in both the TOPAS

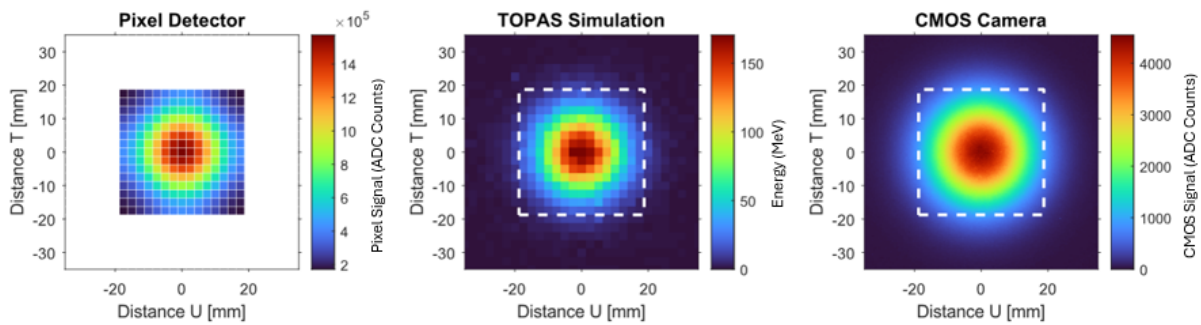


Figure 49: Comparison of 2D profiles for 80 MeV single spots. The white dashed line represents the physical size of a single SPA.

and CMOS ground-truth reconstructions. In the pixel detector, this external signal is wrapped back, resulting in a flawed reconstruction.

Similar conclusions can be drawn by analyzing the 1D spot profiles presented in Figures 50 and 51.

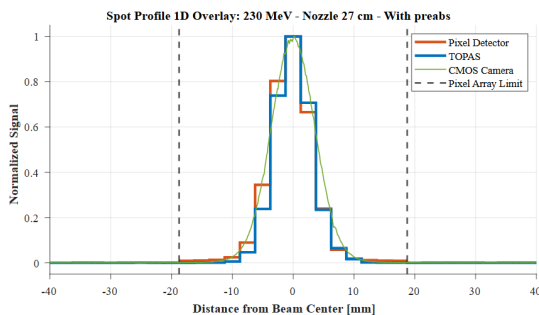


Figure 50: Comparison of 1D profiles for 230 MeV single spots.

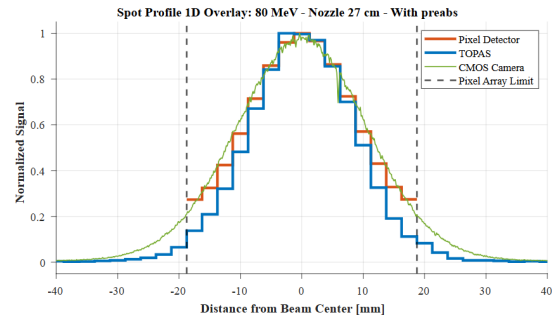


Figure 51: Comparison of 1D profiles for 80 MeV single spots.

5.2 Flatness and Symmetry of Different Fields

An additional test, crucial for both basic data analysis and clinical applications, is the evaluation of the flatness and symmetry of the delivered macroscopic fields. "Flatness" refers to the global uniformity of the detector response across the field plateau. "Symmetry", intuitively, measures how perfectly the dose distribution mirrors itself across the central geometrical axes. It is straightforward to understand why these parameters are critical for patient safety and treatment plan validation.

This analysis was performed on the 10×10 and 20×12 cm² field configurations. For each field, a dedicated MATLAB script extracts a central Region of Interest (ROI). To ensure consistency across different field dimensions, the ROI is dynamically defined by first identifying the Full Width at Half Maximum (FWHM) of the field, and then restricting this area by an additional 20% in both the x and y directions to isolate the pure central plateau.

For the flatness calculation, the algorithm extracts the maximum and minimum signals strictly inside the ROI and computes a percentage variance:

$$f_{\text{Flatness}}(\%) = \frac{\text{Signal}_{\text{high}} - \text{Signal}_{\text{low}}}{\text{Signal}_{\text{high}} + \text{Signal}_{\text{low}}} \cdot 100 \quad (11)$$

Higher values correspond to less uniform fields.

For the symmetry evaluation, the algorithm defines a vertical and a horizontal axis that bisect the ROI, dividing it into perfectly equal halves (upper/lower, left/right). The intersection of these axes highlights a central reference pixel. The algorithm then iterates through every symmetric pixel pair equidistant from the axis, computes the absolute signal difference, and normalizes it against the central reference signal:

$$f_{\text{Symmetry}}(\%) = \frac{\text{Signal}_{\text{left/down}} - \text{Signal}_{\text{right/up}}}{\text{Reference Signal}} \cdot 100 \quad (12)$$

A perfect symmetry corresponds to $f_{\text{Symmetry}} = 0\%$ while increasing values show an increasing asymmetry of the field. The algorithm outputs the maximum calculated variance (representing the worst symmetry point) as the final value for the entire field.

The computed values for flatness and symmetry are reported in Table 2. For the $10 \times 10 \text{ cm}^2$ fields, the flatness and symmetry values are generally on the order of 1% or lower. As expected, slightly worse deviations are observed for the larger $20 \times 12 \text{ cm}^2$ fields.

It is also highly informative to examine the 1D transverse profiles shown in Figures 52,53 for $10 \times 10 \text{ cm}^2$ fields with spot-spacing 2.5 mm, and Figures 54,55 for $20 \times 12 \text{ cm}^2$ fields with spot-spacing 5 mm. It is interesting to notice that a "ripple" structure emerges in the $20 \times 12 \text{ cm}^2$ fields. This geometric artifact originates from the increased 5 mm scanning grid spacing between adjacent spots, which intrinsically limits the absolute flatness of these larger fields compared to the tighter 2.5 mm grid of the smaller fields.

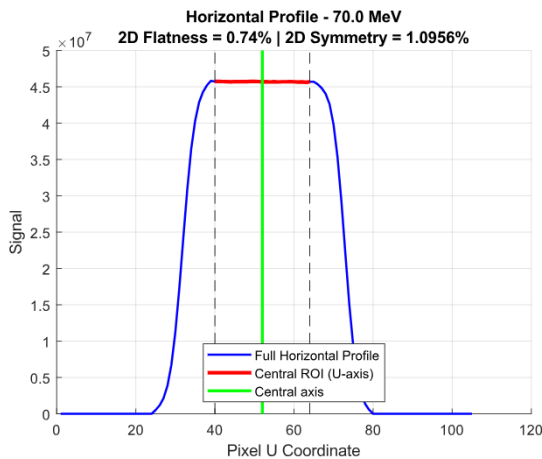


Figure 52: 1D profile of $10 \times 10 \text{ cm}^2$ field at 70 MeV.

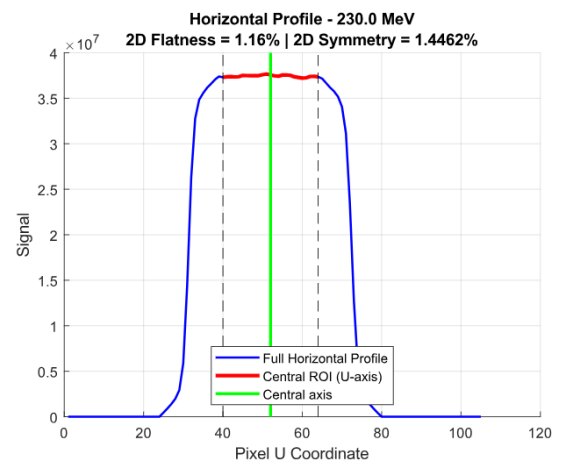


Figure 53: 1D profile of $10 \times 10 \text{ cm}^2$ field at 230 MeV.

A final important feature is demonstrated by the plots in Figures 56,57. These plots show how field flatness slightly deteriorates at higher energies. This degradation is due to the

Energy (MeV)	Flatness (%)	Symmetry (%)
70	0.74	1.10
75	0.78	1.22
80	0.78	1.08
85	0.64	1.01
90	0.66	1.15
100	0.75	1.29
110	0.98	1.45
120	0.78	1.45
130	0.82	1.15
140	0.87	1.22
150	0.80	1.10
160	0.96	1.28
170	0.97	1.17
180	0.95	1.54
190	0.89	1.28
200	0.99	1.23
210	0.98	1.48
220	1.22	1.59
230	1.15	1.45

(a) $10 \times 10 \text{ cm}^2$ field

Table 2: *Experimental Flatness and Symmetry percentage values as a function of the beam energy for both field delivery configurations. Flatness at 0 % means perfect flat field, while Symmetry 0 % means perfect symmetry of the field*

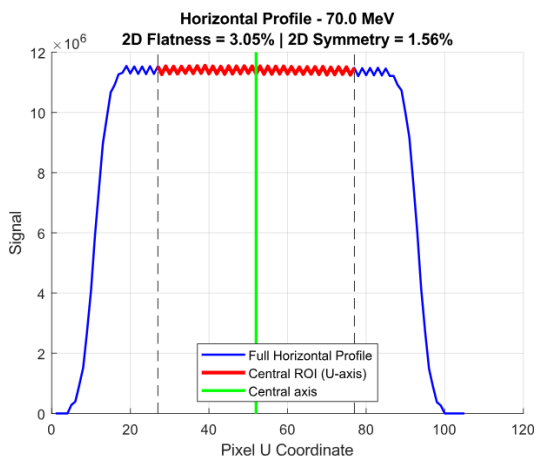


Figure 54: *1D profile of $20 \times 12 \text{ cm}^2$ field at 70 MeV.*

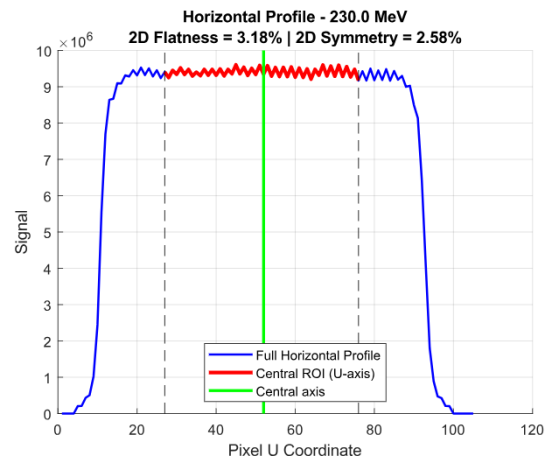


Figure 55: *1D profile of $20 \times 12 \text{ cm}^2$ field at 230 MeV.*

Energy (MeV)	Flatness (%)	Symmetry (%)	Energy (MeV)	Flatness (%)	Symmetry (%)
70	3.05	1.56	155	3.02	1.64
75	2.90	1.43	160	3.17	1.53
80	2.91	1.75	165	3.14	1.47
85	2.72	1.44	170	3.13	1.48
90	2.55	1.57	175	3.02	1.52
95	2.61	1.48	180	3.09	1.68
100	2.67	1.22	185	3.06	1.45
105	2.63	1.48	190	2.87	1.62
110	2.76	1.65	195	3.11	1.54
115	2.70	1.59	200	3.41	1.72
120	2.87	1.83	205	3.24	1.60
125	2.88	1.64	210	3.26	1.76
130	2.98	1.50	215	3.13	1.75
135	2.90	1.35	220	3.31	1.82
140	2.91	1.53	225	3.08	2.01
145	2.90	1.59	230	3.18	2.58
150	3.05	1.43			

(b) $20 \times 12 \text{ cm}^2$ field

Table 2: *Experimental Flatness and Symmetry percentage values as a function of the beam energy for both field delivery configurations. Flatness at 0 % means perfect flat field, while Symmetry 0 % means perfect symmetry of the field*

smaller, more highly focused spots at high energies, which inherently produce less overlap between the Gaussian tails of adjacent spots.

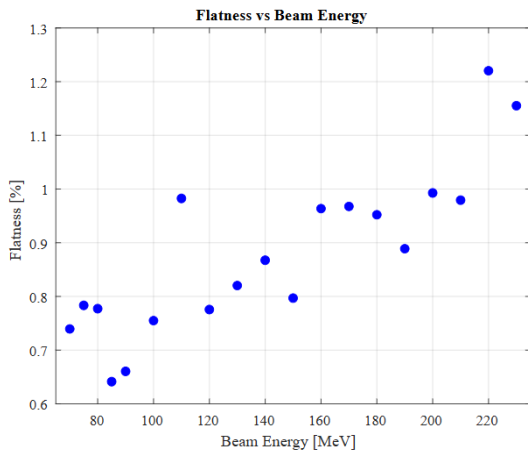


Figure 56: *Flatness values as a function of beam energy for $10 \times 10 \text{ cm}^2$ fields.*

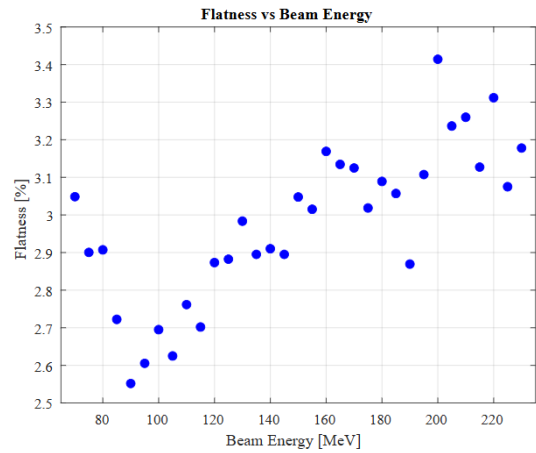


Figure 57: *Flatness values as a function of beam energy for $20 \times 12 \text{ cm}^2$ fields.*

5.3 Dose Calibration

In general, dose calibration consists of finding the mathematical conversion factor required to map the response signal of a given detector (typically expressed in arbitrary analog-to-digital units, ADC) to the absolute physical dose delivered, measured in Gray (Gy).

To achieve this, reference measurements established by an absolute dosimeter are required. Once the absolute dose delivered by a specific reference field is known, measuring the same field with the new detector allows the extraction of the scaling factor. This is the core methodology applied to calibrate the pixel detector.

The absolute reference doses were derived from historical data acquired in 2024 using the Range Scanner (see Section 4.2.2) at exactly 20 mm Water Equivalent Depth (WED). The dataset provides the absolute dose in Gy released by pristine beam layers of different energies. The ultimate goal is to obtain a global scaling factor k , defined as:

$$\text{Scaling Factor } (k) = \frac{\text{Pixel Response Signal}}{\text{Absolute Dose}} [ADC/Gy] \quad (13)$$

For the primary calibration, the homogeneous $10 \times 10 \text{ cm}^2$ fields were used. At the field edges, the dose gradient steeply drops in the so-called "penumbra" region; therefore, it is mandatory to consider only the central, flat plateau. The MATLAB script automatically isolates a central ROI by calculating the FWHM and restricting it inward by an additional 20%. The code computes the mean ADC signal inside this flat ROI and matches it against the reference dose values.

This extraction is performed independently for every energy layer. Subsequently, all the mean responses are multiplied by a common, floating scalar factor k , optimizing the fit to achieve the best possible overlap with the reference dose curve using a Least Squares optimization algorithm. Figure 58 displays the optimally overlapped curves. The best global scaling factor obtained for this setup was $3.12 \times 10^7 \text{ ADC/Gy}$.

To associate a robust statistical error with this calibration, specific scaling factors k_i were computed individually for each energy layer to achieve a perfect 1-to-1 match with the corresponding reference dose. By taking the arithmetic mean and the standard deviation of this array of k_i values, the final calibration constant is defined as:

$$k = (3.128 \pm 0.011) \times 10^7 \text{ ADC/Gy} \quad (14)$$

Figure 59 illustrates the dispersion of the individual k_i values around the mean. Notably, this value is fully compatible with preliminary studies performed the previous year on the same detector using identical modalities, demonstrating excellent hardware reproducibility.

5.3.1 Pressure and Temperature Corrections

An innovative aspect of this study was the systematic evaluation of environmental dependencies. Because the pixel detector is an unsealed ionization chamber, its absolute

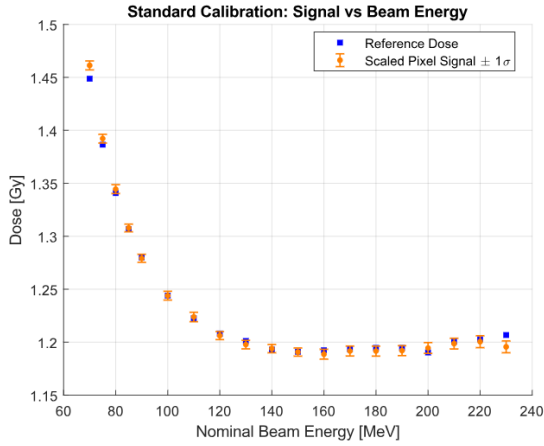


Figure 58: *Scaled signals from the pixel detector fitted to the reference dose points for the $10 \times 10 \text{ cm}^2$ fields.*

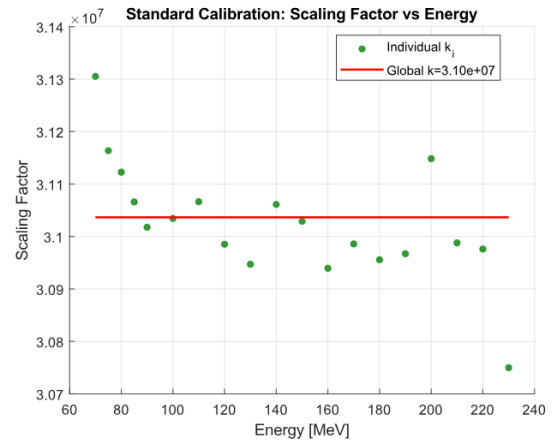


Figure 59: *Individual scaling factors (k_i) evaluated for different energies. The red line represents the global mean k value.*

signal response is strictly proportional to the density of the gas medium inside the air gap. The interaction frequency of the traversing protons is directly modulated by the ambient pressure and temperature [26]. Intuitively, an increase in temperature causes the air density to drop, resulting in a lower measured signal, whereas an increase in pressure compresses the gas, increasing the collision rate and the collected charge.

A standard thermodynamic correction factor (f_{PT}) can be mathematically defined as:

$$f_{PT} = \frac{P_0}{P} \cdot \frac{T}{T_0} \quad (15)$$

where P_0 and T_0 are the reference values at which the reference doses were obtained, and P and T are the environmental values present at the exact time of the measurement.

For this study, the pressure and temperature values recorded during the Range Scanner acquisitions were designated as the reference states P_0 and T_0 . Simultaneously, the internal PT sensor installed inside the pixel detector chassis provided the live P and T telemetry during the new acquisitions. This setup allowed the calculation of dynamic, spot-by-spot correction factors.

The raw ADC response signals were multiplied by their corresponding f_{PT} factor to obtain a normalized, environmentally-corrected signal. Re-running the Least Squares optimization using these corrected signals yielded a refined scaling factor:

$$k_{PT\text{-corrected}} = (3.104 \pm 0.011) \times 10^7 \text{ ADC/Gy} \quad (16)$$

The percentage discrepancy between the raw and the PT -corrected scaling factors is 0.78%, maintaining the variation well below the 1% clinical tolerance threshold, at least in the temperature and pressure ranges used in our measurements. For all subsequent analyses in this thesis, the PT -corrected scaling factor is consistently applied unless otherwise specified.

5.3.2 Spacing Correction

As a purely math exercise, even if not fundamental for the objective of this work, a similar analysis has been repeated over the large $20 \times 12 \text{ cm}^2$ fields.

However, a critical physical difference must be addressed. In the large fields, the proton spots were delivered on a 5 mm grid, whereas the small fields utilized a tighter 2.5 mm grid. This wider spacing implies significantly less overlap between the Gaussian tails of adjacent spots, resulting in a lower integrated plateau signal. Consequently, applying the raw scaling factor k derived from the 2.5 mm grid would intrinsically underestimate the dose of the 5 mm field. Moreover, since spot width varies heavily with energy, the severity of this amplitude drop is energy-dependent. This geometric effect is clearly illustrated in Figures 60, 61 and 62.

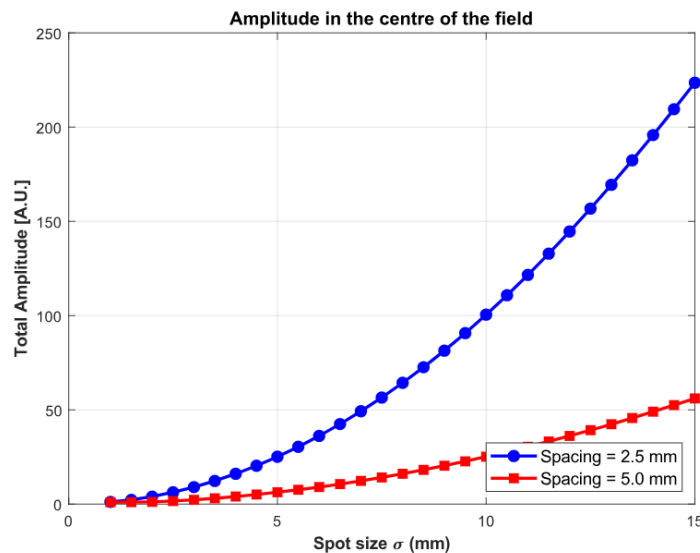


Figure 60: *Theoretical plateau amplitude at the center of a Gaussian grid as a function of the single spot σ , comparing the two spacing configurations.*

To compensate for this structural lack of overlap, an analytical "spacing correction factor" was developed. A custom MATLAB routine was implemented to generate synthetic mathematical grids of 2D Gaussians, replicating the exact delivery patterns of the 2.5 mm and 5 mm fields. The algorithm systematically iterates through different single-spot σ values (from 1 mm to 15 mm, covering the full physical spectrum of the clinical beam). For each simulated σ , it calculates the ratio between the theoretical maximum amplitude achieved by the 2.5 mm grid and the one achieved by the 5 mm grid. This ratio represents the exact "amplitude loss" factor specific to that spot width.

During the experimental analysis, a second script parses the actual data log of the large field, extracting the true σ_x and σ_y of the delivered spots. It computes the Root Mean Square (RMS) of these sigmas to obtain a single representative width for that specific energy layer. Using this real σ value, the script interpolates the synthetic grid data to extract the corresponding mathematical spacing correction factor.

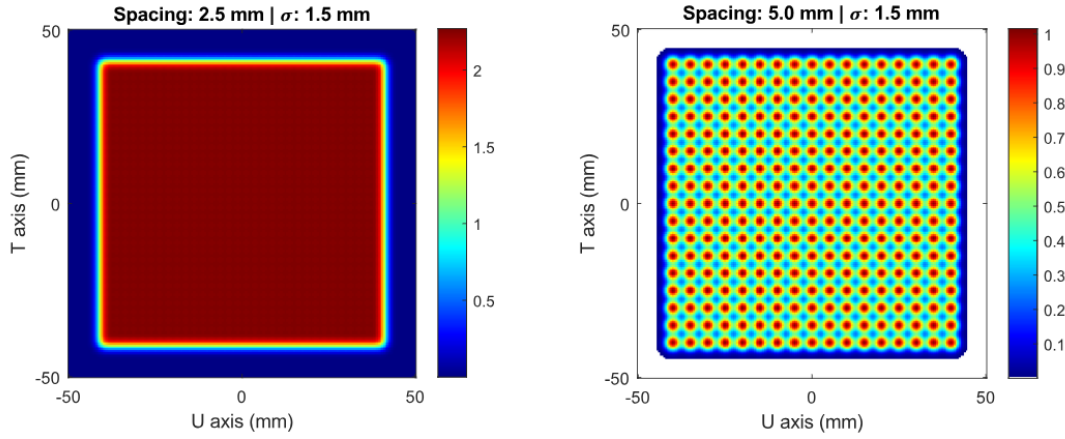


Figure 61: *2D comparison of the dose topology for a grid of spots ($\sigma = 1.5$ mm) delivered with 2.5 mm and 5 mm spacing.*

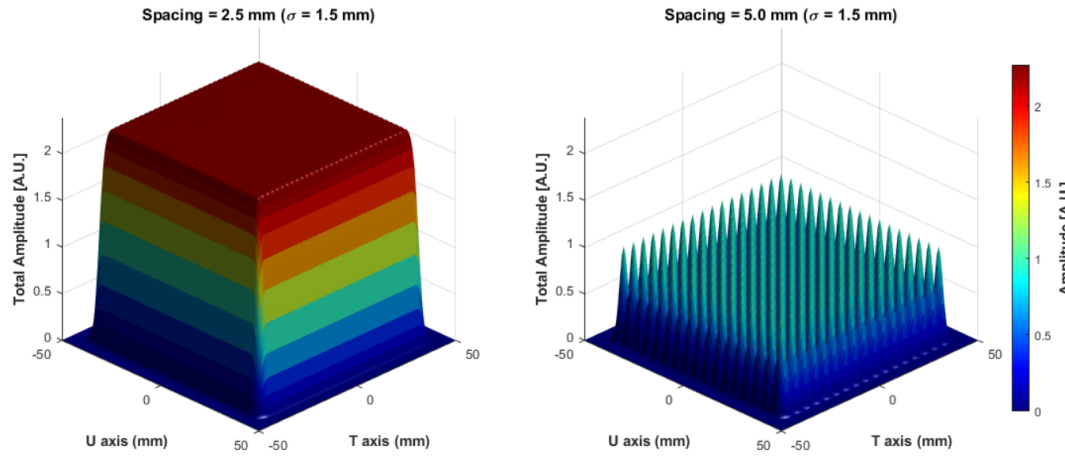


Figure 62: *3D rendering of the dose topography for the two different scanning grids, demonstrating the severe loss of total amplitude at wider spacings.*

This geometric spacing factor is then multiplied by the raw experimental signal, alongside the thermodynamic PT correction. From this point onward, the calibration workflow proceeds identically to the small fields. The newly obtained, fully corrected scaling factor for the large fields is:

$$k_{PT+Spacing} = (3.099 \pm 0.025) \times 10^7 \text{ ADC/Gy} \quad (17)$$

This value is in excellent statistical agreement with the calibration factor obtained from the tightly spaced small fields, definitively proving the validity of the numerical correction model.

5.4 Dose Box Validation

A rigorous clinical verification of the calculated scaling factor was performed using the standard $6 \times 6 \times 6$ cm³ Dose Box. This complex 3D field is designed to deliver a flat,

uniform dose of exactly 1 Gy throughout the plateau of the Spread-Out Bragg Peak (SOBP) (see Section 4.1.4).

By converting the raw ADC maps acquired by the pixel detector using the scaling factor, the absolute reconstructed dose can be directly benchmarked against the expected 1 Gy threshold. To thoroughly map the SOBP, data were acquired at various longitudinal PMMA depths (2.3, 3.3, 4.3, 5.3, 6.3, and 7.3 cm) both with and without the pre-absorber. The true geometric center of the SOBP is located at exactly 7.3 cm.

A preliminary qualitative study confirmed that the macroscopic structure of the field, as well as the individual energy layers, were correctly reconstructed. Figure 63 provides examples of the integrated fields at selected depths.

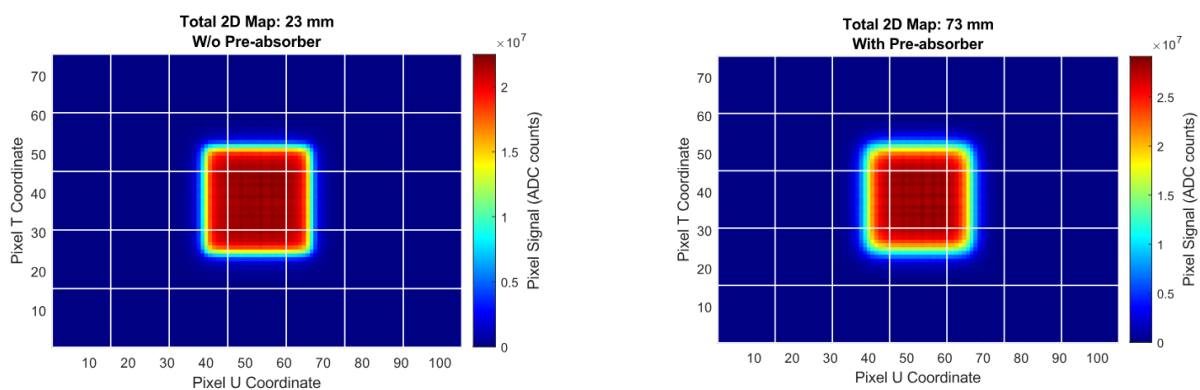


Figure 63: *Total reconstructed dose fields for the Dose Box at different longitudinal depths.*

The integrated field structure appears correct. As physically expected, the lowest energy layers fail to reconstruct correctly at deeper PMMA depths because their primary protons stop before reaching the detector scoring plane. Figure 64 highlights examples of these "empty" reconstructions at the tail end of the Bragg peak ranges.

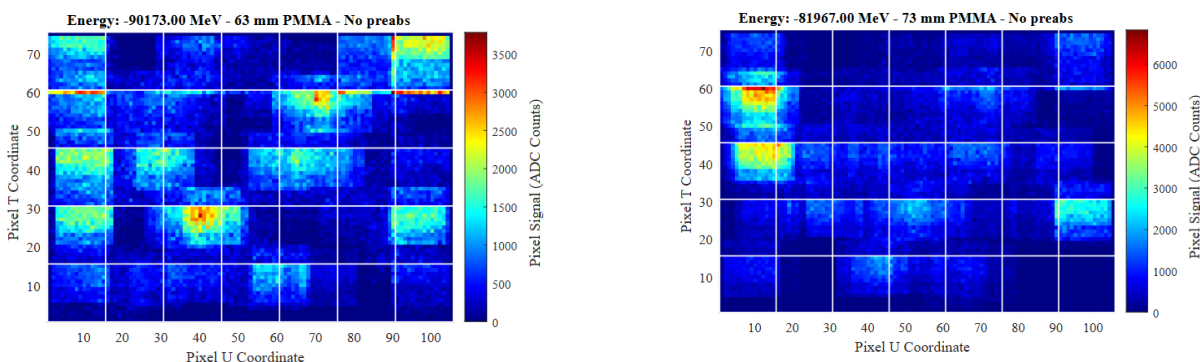


Figure 64: *Examples of expected signal loss for low-energy spot layers reaching the end of their physical range inside the Dose Box.*

Moving to the absolute dose analysis, the central uniform ROI of the total Dose Box field is extracted using the exact same MATLAB routines applied during the basic calibration. The average raw signal inside the ROI is thermodynamically corrected via f_{PT} and finally

multiplied by the global scaling factor k to yield the absolute dose in Gray. The results for all the investigated depths are summarized in Table 3.

Depth (cm)	Dose w/o pre-absorber (Gy)	Dose with pre-absorber (Gy)
2.3	0.7041	0.7395
3.3	0.7635	0.7975
4.3	0.8637	0.9131
5.3	0.9057	0.9236
6.3	0.8932	0.9105
7.3	0.9019	0.9091

Table 3: *Absolute reconstructed dose values measured in the central plateau of the $6 \times 6 \times 6$ cm³ Dose Box at different PMMA depths.*

These numerical results immediately reveal a severe, systematic discrepancy. Specifically, at the 7.3 cm depth (the geometric center of the SOBP plateau), the detector should register exactly 1.0 Gy, yet the calibrated reconstruction stalls around 0.9 Gy.

To investigate this alarming underestimation, the detailed TOPAS simulations of the Dose Box (Section 4.3.3) were consulted. The Monte Carlo data confirmed that the theoretical dose delivery is indeed a perfectly flat 1.0 Gy across the center of the plateau. By plotting the experimental pixel detector doses alongside the TOPAS benchmark curve, a massive, global underestimation of the absolute dose becomes blatantly apparent (see Figure 65). Included in this plot are the normalized signals obtained from the CMOS camera (Section 4.2.1), serving strictly as an independent geometric verification of the expected SOBP plateau shape, not for absolute dosimetry.

To confirm this anomaly transversely, 1D lateral profiles of the macroscopic field were extracted from both the pixel detector arrays and the TOPAS matrices. Examples at selected depths are shown in Figure 66.

A systematic amplitude deficit on the order of 10% plagues every single configuration, both with and without the pre-absorber. This provides definitive evidence of an intrinsic structural flaw in the simple linear dose conversion algorithm when applied to highly complex, mixed-energy fields.

5.5 Patient's Treatment Plans Validation

A definitive "real-world" stress test for the pixel detector's response was conducted by attempting to reconstruct actual clinical patient treatment plans. As described in Section 4.1.5, two heavily modulated non-uniform fields (F0 and F1) were exported directly from the TPS and delivered onto the pixel detector. Following the established pipeline, the 2D dose maps were reconstructed and subsequently benchmarked against the native TPS projections. Figure 67 presents side-by-side examples of these complex fields.

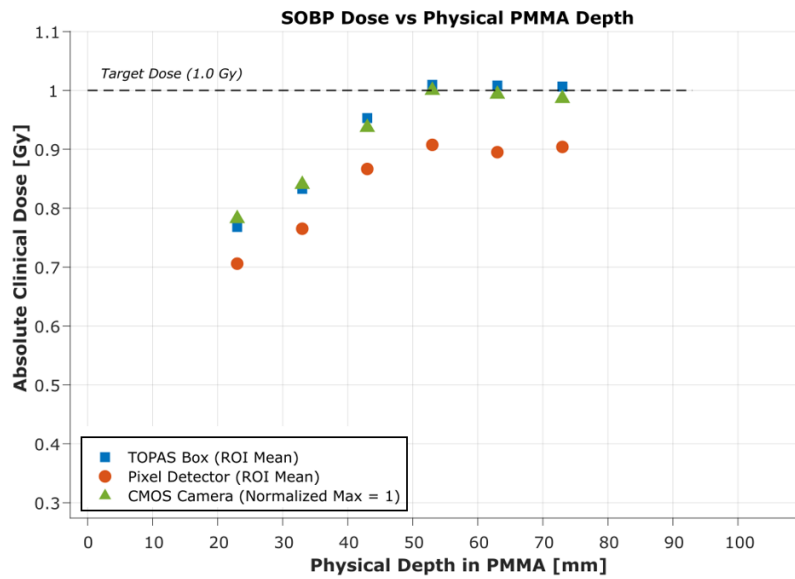


Figure 65: *Longitudinal comparison of the reconstructed SOBP. The pixel detector severely underestimates the absolute 1.0 Gy plateau established by the TOPAS ground-truth. The CMOS data serves as a shape reference.*

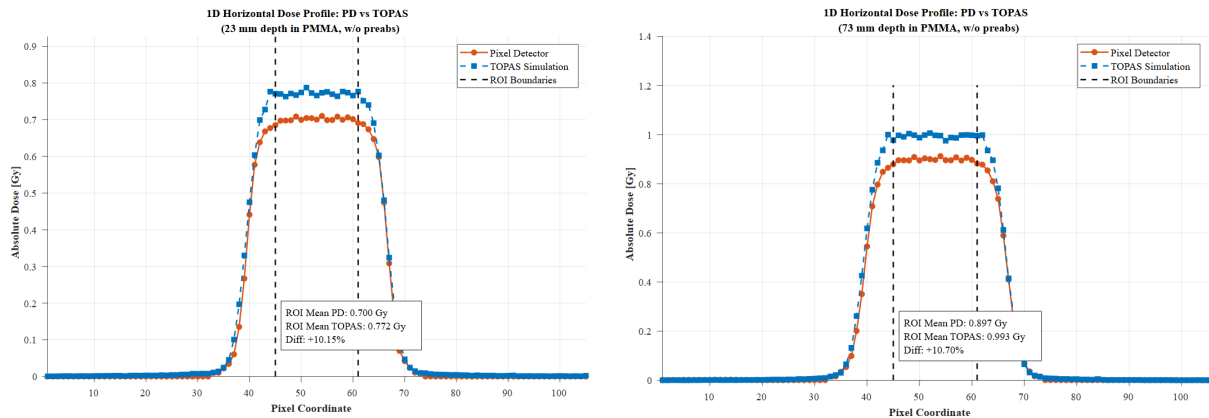


Figure 66: *1D transverse profile comparisons between the TOPAS simulations and the pixel detector data, highlighting the systematic amplitude loss.*

The TPS provides the expected reference dose matrices at three specific depths in water: 1.16 cm, 1.635 cm, and 4.555 cm. These depths mathematically perfectly match the PMMA slab configurations used during the physical data acquisition.

To perform a rigorous pixel-by-pixel comparative analysis, a resolution mismatch had to be solved. The clinical TPS grid utilizes a coarse 4 mm pitch, whereas the pixel detector boasts a finer 2.5 mm pitch. To align the matrices, the MATLAB script performs a 2D bilinear interpolation on the coarse TPS data, resampling it to perfectly match the 2.5 mm grid of the detector. Once the matrices are spatially aligned, the algorithm subtracts the reconstructed detector dose from the TPS reference dose. Figure 68 maps the relative percentage differences for all three investigated depths.

The error maps consistently display blue regions at the borders, consisting in dose gradient

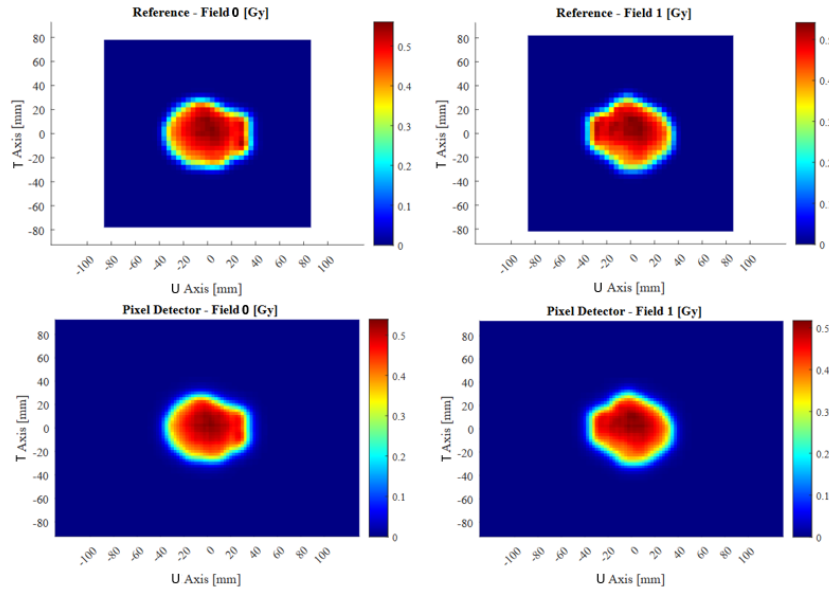


Figure 67: *Visual comparison between the expected 2D dose maps generated by the TPS and the experimental fields reconstructed by the pixel detector (1 cm depth).*

regions where errors can be very large due to resolution. The interesting part are the red regions inside the field that indicate a systemic dose deficit on the order of 5% to 10% across vast portions of the fields. This finding rigidly confirms the hypothesis raised by the Dose Box experiment: the pixel detector inherently underestimates the absolute delivered dose even at very shallow depths.

5.6 Bragg Peak Scan Validation

The final, definitive diagnostic test to understand the detector's anomalous behavior was the reconstruction of pristine depth-dose curves (Bragg peak scans). Figure 69 shows the experimental longitudinal profiles acquired by the pixel detector.

Despite the relatively coarse longitudinal sampling resolution, the plots broadly trace the fundamental physics of the Bragg peak. Disregarding the first three curves (70, 80, and 90 MeV), the peak signal correctly scales down as the nominal beam energy increases. The anomaly in the lowest energy peaks is an experimental artifact: their Bragg peaks are so incredibly sharp and narrow that hitting the exact peak depth with finite PMMA slabs is statistically improbable, resulting in "clipped" measurements.

To genuinely validate the detector's operational fidelity, these curves must be benchmarked against the gold-standard data from the Range Scanner (Figure 70).

Beyond the obvious difference in raw signal amplitude units, a structural difference exists at the entry plateau of the curves. The Range Scanner curves perfectly overlap at the entrance window, whereas the pixel detector curves show higher entrance signals for lower energy beams. This is not a detector flaw, but a programmatic difference in the

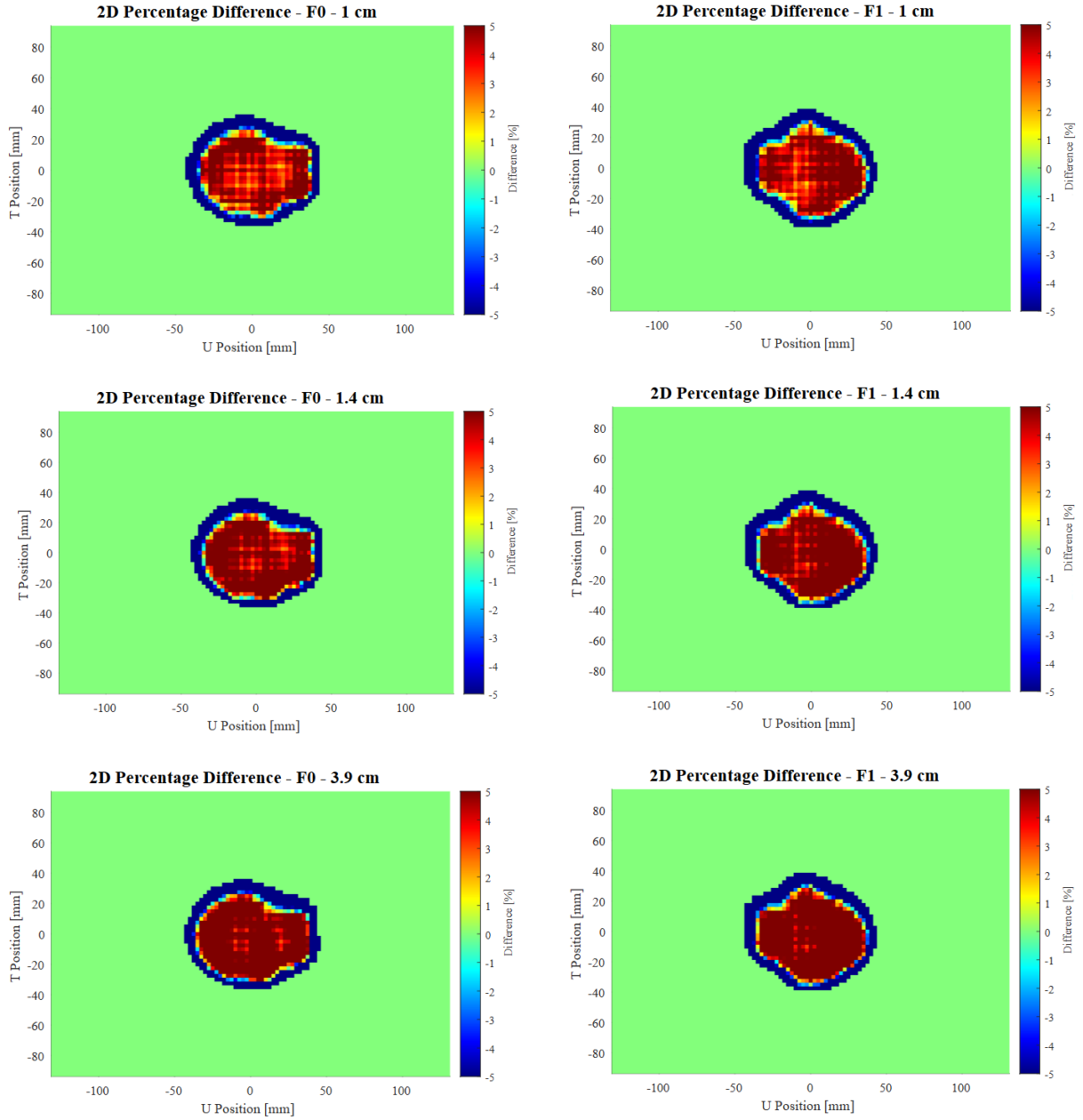


Figure 68: 2D spatial maps detailing the relative percentage discrepancy between the TPS ground-truth and the pixel detector reconstructions.

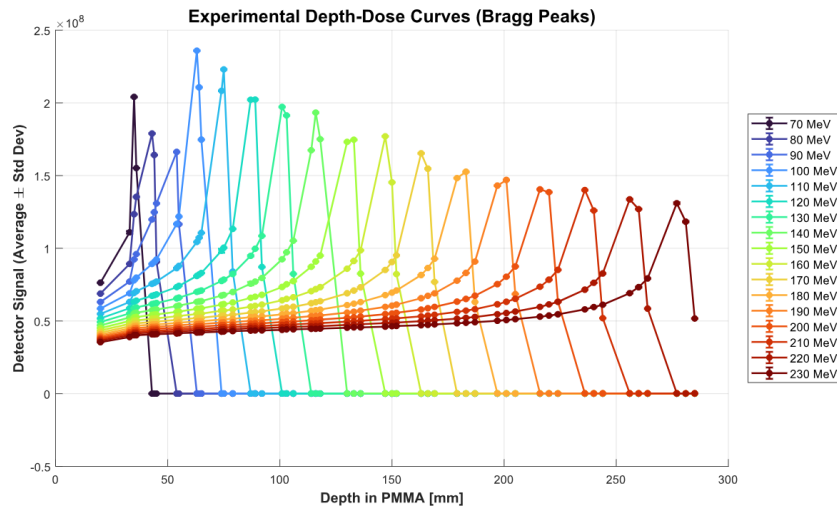


Figure 69: *Raw depth-dose curves reconstructed from the experimental points acquired by the pixel detector.*

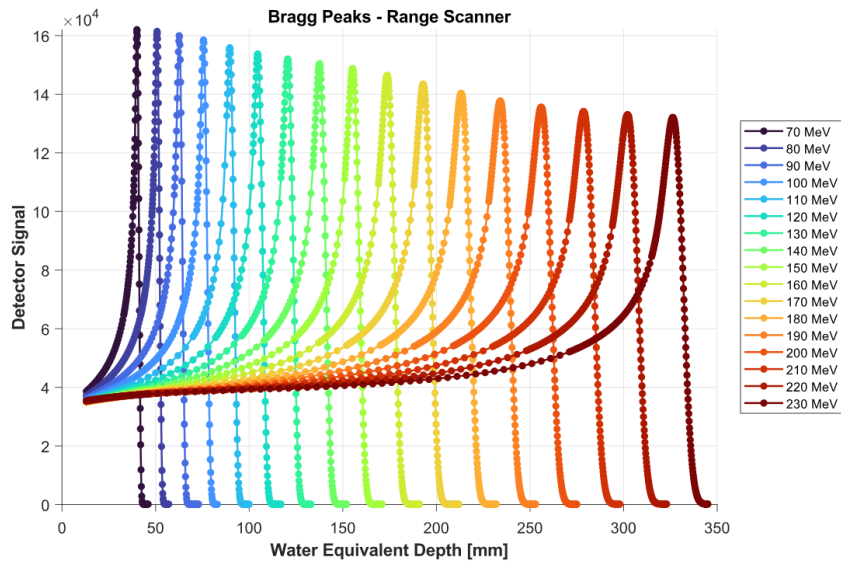


Figure 70: *High-resolution reference depth-dose curves acquired with the Range Scanner (2024 data).*

beam delivery protocols. During the Range Scanner calibration runs, the TCS artificially equalizes the entrance current for all energies. During the pixel detector runs, the raw beam physics dictate the entrance current.

A second logistical mismatch involves the phantom materials. The pixel detector positions represent physical depth in PMMA, whereas the Range Scanner logs represent depth in pure water. To allow a 1-to-1 comparison, the water depths were mathematically converted into PMMA equivalent depths using the strict ratio of their stopping powers.

Once geometrically aligned in PMMA space, the pixel detector curves were scalar-multiplied to force their very first entry point (the most superficial depth) to perfectly overlap the

corresponding entry point of the Range Scanner data. The result of this alignment is presented in Figure 71.

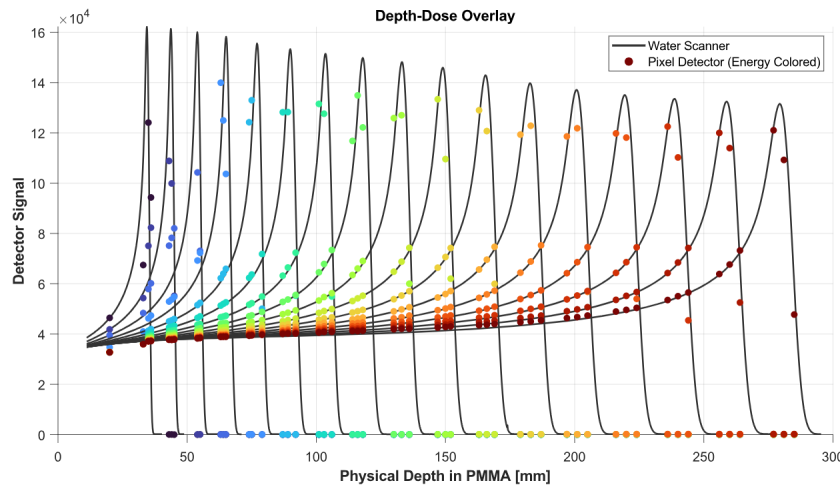


Figure 71: *Superposition of the Range Scanner and Pixel Detector depth-dose curves. The detector curves are scaled to artificially match the plateau entrance signal of the reference data.*

This comparative plot reveals a not perfect matching. The pixel detector curves do not track the reference data. Specifically, at higher energies, the pixel detector curves appear physically "shifted" to the left (towards shallower depths), and the amplitude of the Bragg peak is drastically amputated compared to the Range Scanner ground truth.

To dissect this phenomenon with higher precision, a dedicated, high-resolution scan was performed strictly for the 150 MeV beam, sampling points at sub-millimeter intervals around the expected Bragg peak. Figure 72 isolates these experimental points.

This high-resolution overlay indisputably confirms the hypothesis. The pixel detector curve is geometrically shifted backward and suffers a severe loss of signal amplitude exactly inside the Bragg peak region. This proves that the simplistic dose conversion model is fundamentally incapable of resolving the dense energy deposition dynamics occurring at the end of the proton range.

5.7 Material Budget Considerations

As meticulously described in Chapter 1, the internal architecture of the pixel detector consists of 4 distinct cathodic layers sandwiched around a massive PCB supporting structure. The total electronic signal read by the software is the blind sum of the ionization events occurring in both the top and bottom air gaps.

When a proton traverses the detector, it deposits a fraction of its energy in the top air gap, then travels through the dense, inactive PCB stack (losing kinetic energy), and finally

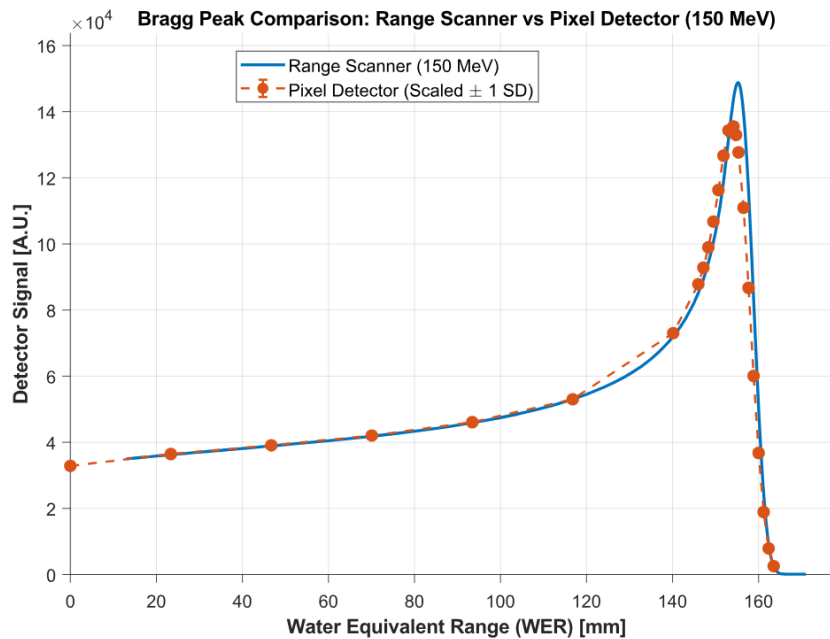


Figure 72: *High-resolution overlap for the 150 MeV beam. The pixel detector curve is scaled to match the entrance plateau of the reference curve.*

deposits more energy in the bottom air gap. Because the proton slows down considerably inside the thick PCB, the top and bottom air gaps are effectively measuring protons at two different energy states.

In Section 4.4, simulations demonstrated that for single pristine spots far away from the Bragg peak (in the flat entry plateau), the physical presence of the PCB does not significantly corrupt the total signal. However, if this internal material budget is analyzed in the context of a Bragg peak scan, the scenario changes significantly. The schematic in Figure 73 visually explains why the PCB structure annihilates the signal collection at the end of the proton range.

The PCB stack equates to roughly 3.2 mm of WET. If the proton beam is specifically tuned so that its Bragg peak (the point of maximum energy deposition and subsequent complete stop) falls exactly within those 3.2 mm of dead PCB material, the proton will heavily ionize the top air gap, crash into the PCB, and never reach the bottom air gap. Losing 50% of the active detection volume exactly where the dose is highest inevitably results in a massive, systemic underestimation of the delivered dose.

To empirically test this "PCB shadowing" theory, a simple, non-rigorous mathematical manipulation was performed. Referring back to the high-resolution 150 MeV curve (Figure 72), the pristine Range Scanner curve was taken, duplicated, and geometrically shifted by exactly 3.2 mm towards shallower depths. The arithmetic mean between the original curve and the shifted curve was then calculated to create a synthetic "composite" depth-dose profile (Figure 74).

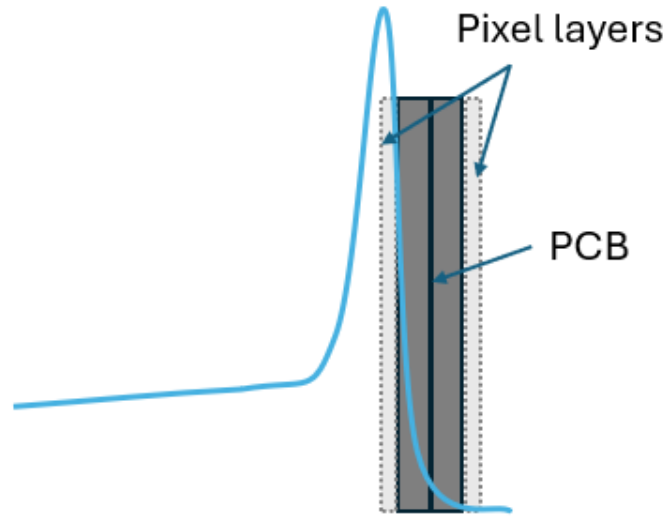


Figure 73: *Schematic representation of the PCB "shadowing" effect. Protons stopping inside the dead PCB material completely fail to trigger the bottom air gap, destroying the total collected signal.*

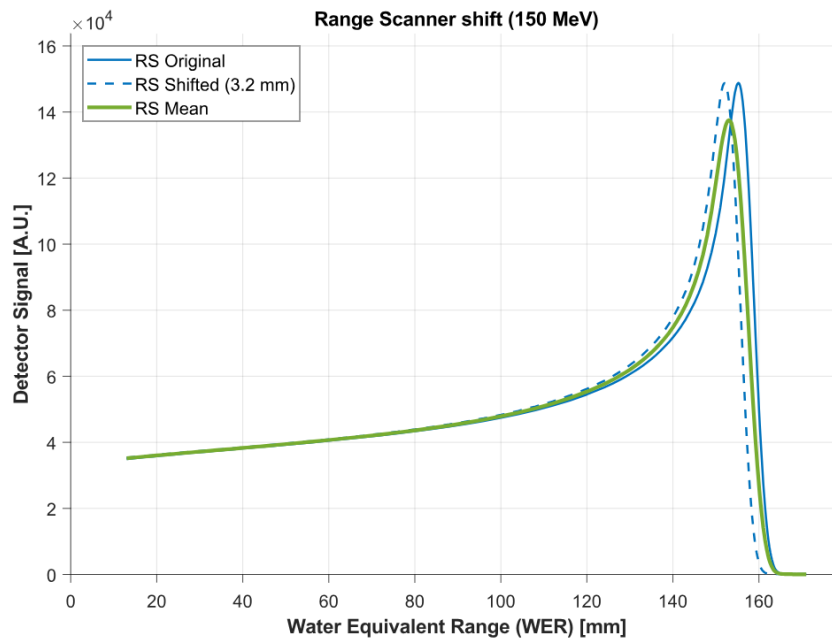


Figure 74: *Synthetic composition averaging a pristine Range Scanner curve with a 3.2 mm shifted copy.*

The defining moment occurs when this crude synthetic curve is overlaid on top of the struggling pixel detector data. As shown in Figure 75, the two curves fit perfectly.

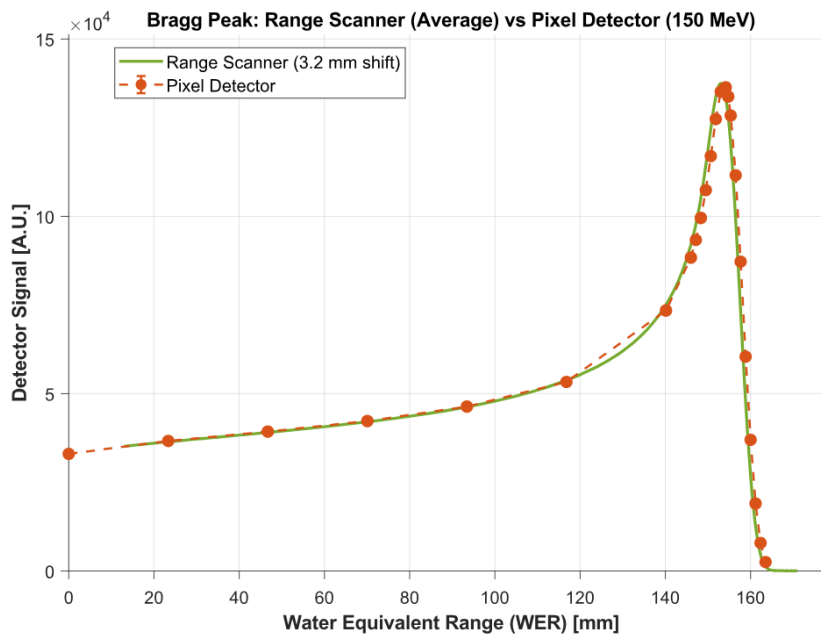


Figure 75: *Perfect overlap between the synthetic "shadowed" reference curve and the raw experimental data from the pixel detector.*

Although mathematically simplistic, this manipulation provides absolute smoking-gun evidence. The 3.2 mm thickness of the PCB is entirely responsible for the signal loss. Any accurate dosimetric calibration of this detector must inherently account for this massive internal material budget.

With the root cause identified, a final series of TOPAS simulations was executed to verify if this PCB shadowing effect was also responsible for the systemic 10% dose underestimation observed during the complex Dose Box and Patient Plan validations.

As outlined in Section 4.4, earlier simulations utilized a compromised geometry featuring only a single scoring layer. A brand-new TOPAS geometry was coded, explicitly introducing a second, fully functional virtual scoring layer. These two layers were separated by a dead water tank precisely matching the 3.2 mm WET of the real PCB (see Figure 43:d). In this highly accurate simulation, TOPAS independently calculates the dose deposited in both the top and bottom layers, and MATLAB averages them, perfectly mirroring the real hardware electronics.

Figures 76 and 77 present the outcome of the Dose Box reconstructed using this advanced, double-layer simulation geometry.

The results of this final test are not conclusive. In the configurations without the pre-absorber (pure, unscattered beam), the advanced simulation still stubbornly predicted a flat 1.0 Gy dose delivery. This means that, for pristine beams, the inclusion of the 3.2 mm

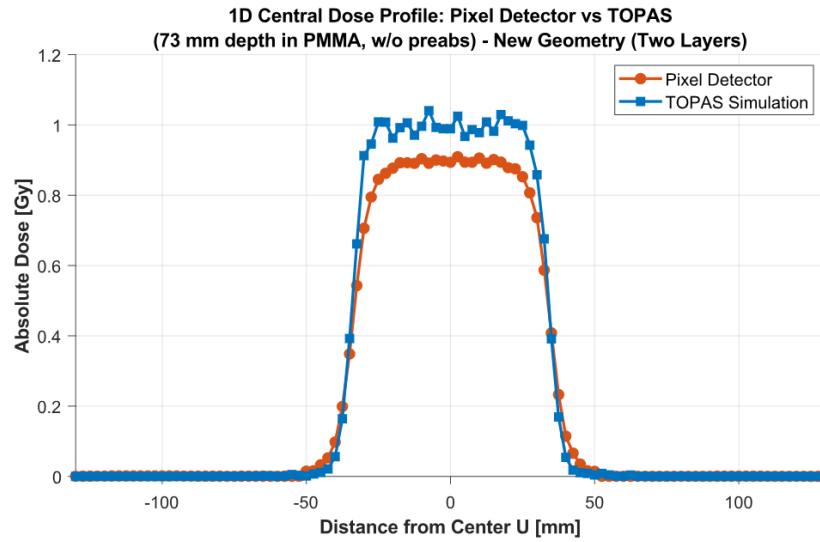


Figure 76: 1D profile comparison of the Dose Box (73 mm depth, no pre-absorber). The advanced double-layer TOPAS simulation (dashed line) still predicts 1.0 Gy, failing to explain the pixel detector's signal loss.

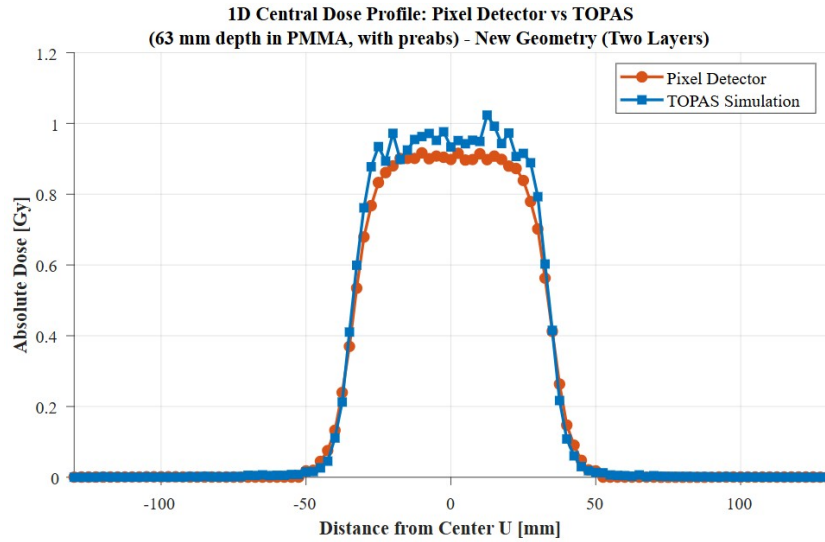


Figure 77: 1D profile comparison of the Dose Box (63 mm depth, with pre-absorber). The advanced double-layer TOPAS simulation correctly predicts a lower dose, aligning much better with the experimental data.

dead space in the simulation had almost zero effect on the macroscopic SOBP plateau, proving that the PCB shadowing cannot be the sole culprit for the missing 10% dose.

Conversely, in configurations featuring the pre-absorber (highly scattered, complex beam), the advanced simulation accurately registered a significant dose drop in the plateau, aligning much closer with the experimental pixel detector data.

In conclusion, these extensive tests prove that while the massive internal geometry of the detector severely distorts measurements near the Bragg peak, it is likely not the only source of error. Further investigations and far more sophisticated Monte Carlo modeling are required to unlock the detector's true dosimetric potential.

Conclusions

Proton therapy, particularly when delivered via Pencil Beam Scanning (PBS) as used at the Paul Scherrer Institute (PSI), represents a highly advanced modality for conformal cancer treatment. However, as discussed in the initial chapters of this thesis, the extreme precision of PBS and Intensity-Modulated Proton Therapy (IMPT) demands equally precise and efficient Quality Assurance (QA) procedures. The development of high-resolution 2D detectors is crucial to streamline this workflow, reduce treatment dead-time, and guarantee patient safety. This thesis investigated the dosimetric performance and absolute dose calibration of a novel pixel detector system designed specifically to address these clinical QA requirements at the Gantry 2 facility.

The main results obtained during this project concern the formal dose calibration of the pixel detector. As outlined in Section 5.3, the baseline procedure led to a scaling factor of:

$$k = (3.128 \pm 0.011) \times 10^7 \text{ ADC/Gy} \quad (18)$$

This value is in excellent agreement with the results obtained using a similar procedure during previous preliminary studies, successfully demonstrating the reproducibility of the measurements.

A more in-depth study was performed to account for the thermodynamic variations of the gas medium (pressure and temperature). With this correction applied, the refined scaling factor was found to be:

$$k = (3.104 \pm 0.011) \times 10^7 \text{ ADC/Gy} \quad (19)$$

This demonstrates a pressure-temperature (PT) effect of less than 1% in our working conditions. Furthermore, a highly compatible scaling factor was obtained when evaluating larger fields, such as the $20 \times 12 \text{ cm}^2$ configuration, by successfully applying the developed geometric spacing corrections.

Despite the high reproducibility of the baseline calibrations, applying the resulting scaling factor to complex, clinically relevant irradiation fields remains challenging for several reasons. The calibration data were acquired at a constant particle rate and, in most cases, at a fixed beam energy. By contrast, clinical treatments employ multiple beam energies, with particular attention required in the Bragg-peak region, where ionization reaches its maximum and the detector response becomes especially sensitive to detector-specific characteristics, particularly its geometry. Indeed, when the detector was used for quality assurance in clinical tests, its response was approximately 10% lower than expected for the dose-box measurements and 5% lower for the patient treatment plans. These discrepancies exceed the stringent tolerance limits required in a clinical quality-assurance environment.

By analyzing the depth-dose curves across different energies, a new investigative approach was adopted to understand these discrepancies. Evaluating the material budget between

the pixel cathodic layers revealed that the Printed Circuit Board (PCB) significantly affects the measurements, particularly in the Bragg peak region. While incorporating this hardware limitation into the simulations proved highly effective for a single pristine depth-dose curve, applying the same logic to the Dose Box simulations yielded only partial corrections. In the highly-scattered configuration (with the pre-absorber inserted), the PCB effect explains only partially the observed 10% dose deviation.

In conclusion, as discussed in previous sections, under the pencil-beam conditions employed at PSI, the current pixel detector demonstrates excellent spatial resolution in reconstructing the delivered proton spots. It also provides an accurate measurement of the energy deposited in the detector for proton energies above 70 MeV. However, several limitations emerge outside these operating conditions:

- As outlined in Section 5.1, large beam spots are subject to substantial spatial misreconstruction because of the channel-recycling technique implemented in the readout electronics. Further investigation is required to determine whether, in addition to the loss of spatial-profile information, the signal generated in regions outside the central Small Pixel Array (SPA) is only partially collected. Analytical modeling should therefore be used to quantify the potential signal loss associated with large spots, as this effect may constitute an additional source of error contributing to the overall dose underestimation observed with the pixel detector.
- At very low proton energies, particularly near the Bragg peak, the assumption that the two sides of the detector produce equivalent signals is no longer valid because protons traverse different material budgets before reaching the respective sensing layers. Under these conditions, the detector response becomes nonlinear, thereby reducing the accuracy of the calibration. Several possible solutions could be explored in future work: (a) developing an optimized detector design with a thinner printed circuit board between the cathodic layers; (b) implementing a dedicated algorithm to mathematically disentangle the signals originating from the upper and lower pixel layers; (c) reading out the two layers independently; or (d) using only a single detection layer. Among these alternatives, the last appears to offer the simplest and most effective solution.

This work presented the first comprehensive characterization of the detector and identified its optimal operating conditions as a pass-through beam monitor, demonstrating its high stability and excellent spatial resolution. It also revealed intrinsic limitations affecting its application as a quality-assurance monitor near the Bragg peak and outlined some research directions to be pursued in future studies.

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Appendix

Water Equivalent Thickness

In radiotherapy and particle therapy, it is common practice to express the thickness of objects in terms of Water Equivalent Thickness (WET), i.e. the thickness that an element of a generic material would have if it were entirely composed of water while maintaining the same overall stopping power. In this context, everything, from detector components to proton ranges, is often expressed in terms of WET.

The reason for this convention is that the human body is mainly composed of water, approximately 60%, depending on age, sex, and body weight. During a treatment, most of the material encountered by the particles along their path, where they deposit their energy, is therefore water.

For this reason, it is convenient to use the WET when discussing particle ranges, especially proton ranges. In proton therapy, it becomes particularly important to know how to convert a physical length into its water-equivalent thickness.

First of all, recall that the stopping power is defined as the quantity dE/dx , which represents the energy lost by charged particles while traversing a material. This quantity follows the Bethe–Bloch formula introduced in Chapter 1. Different materials affect traversing particles differently, causing them to deposit energy at different rates. Often, the mass stopping power is used, which is simply the stopping power divided by the density of the material [27].

As mentioned before, the idea is to determine the thickness that a particular object would have if it were made of water instead of its actual material while preserving the same stopping capability. To do so, the following expression can be used:

$$t_w = t_m \cdot \frac{\rho_m}{\rho_w} \cdot \frac{S_m/\rho_m}{S_w/\rho_w} \quad (20)$$

where t_m is the original thickness of the material (the subscript m stands for “material”), t_w is the corresponding thickness in water, $\rho_{m,w}$ are the densities of the material and water, and S_m/ρ_m and S_w/ρ_w are their respective mass stopping powers.

As an example, consider the pre-absorber block of the Gantry 2 nozzle. This is a graphite block approximately 2.7 cm thick. To compute its WET, it is first necessary to determine the values of the parameters appearing in the previous formula. Proton ranges in different materials, stopping power values at different energies, and many other data can be obtained from the PSTAR tables provided by the National Institute of Standards and Technology (NIST) [28]. For example, at 70 MeV, the values $S_g/\rho_g = 8.553 \text{ MeVcm}^2/\text{g}$ and $S_w/\rho_w = 9.559 \text{ MeVcm}^2/\text{g}$ are obtained. Knowing that the densities of graphite and

water are $\rho_g = 1.7 \text{ g/cm}^3$ and $\rho_w = 1.0 \text{ g/cm}^3$, respectively, we can directly apply Eq. 20 to obtain the WET of the pre-absorber:

$$t_w = 2.7 \text{ cm} \cdot \frac{1.7 \text{ g/cm}^3}{1.0 \text{ g/cm}^3} \cdot \frac{8.553 \text{ MeVcm}^2/\text{g}}{9.559 \text{ MeVcm}^2/\text{g}} \simeq 4.2, \text{ cm}. \quad (21)$$

This result is in agreement with the value of 4.2, cm WET used throughout this thesis.

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