

Water calorimetry for accurate dosimetry of advanced hadron therapy modalities

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Abstract

Advanced radiotherapy modalities such as proton, carbon and helium ion therapy may offer advantages compared to conventional photon therapy due to their characteristic Bragg peak, which allows most of the dose to be deposited at a well-defined depth. In addition, light ion therapy may benefit from an increased biological effectiveness. Accurate dosimetry is therefore essential to ensure safe and effective treatment delivery. In clinical reference dosimetry, absorbed dose to water is typically measured using ionization chambers calibrated in a reference beam quality and corrected for differences in radiation quality using a beam quality correction factor, k_Q . While reference dosimetry for high-energy photon beams is well established, uncertainties associated with absorbed dose measurements remain larger for proton, carbon and helium ion beams, mainly due to the limited availability of experimentally determined k_Q -factors. The aim of this thesis was to reduce uncertainties in reference dosimetry for advanced radiotherapy modalities using water calorimetry, the most direct method for determining absorbed dose to water. Beam quality correction factors were experimentally determined for several ionization chamber types in high-energy photon, proton, carbon and helium ion beams. The measurements provide experimental validation of current recommendations in international dosimetry protocols for proton beams and substantially expand the available experimental database of k_Q -factors for carbon ion beams. For helium ion beams, this work provides the first experimentally determined k_Q -factors. In addition, a direct comparison between the water calorimeter and a graphite calorimeter developed at the National Physical Laboratory was performed in carbon ion beams, providing an important cross-validation between independent calorimetric techniques. The results of this thesis strengthen the experimental foundation of reference dosimetry for particle therapy and contribute to improving the accuracy and reliability of absorbed dose measurements in advanced radiotherapy modalities.

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List of abbreviations

AAPM		American Association of Physicists in Medicine
BIPM		Bureau International des Poids et Mesures
CoP		Code of Practice
CT		Computed Tomography
FEM		Finite element method
FFF		Flattening Filter Free
IAEA		International Atomic Energy Agency
IC		Ionization chamber
IMRT		Intensity-modulated radiation therapy
LET		Linear energy transfer
MRI		magnetic Resonance Imaging
MU		Monitor units
MV		Megavoltage
NPL		National Physical Laboratory
NTCP		Normal Tissue Complication Probability
PDD		Percentage depth dose
PMMA		Poly(methyl methacrylate)
PBS		Pencil beam scanning
PSDL		Primary Standards Dosimetry Laboratory
PTFE		Polytetrafluorethylene
PTB		Physikalisch-Technische Bundesanstalt
RBE		Relative biological effectiveness
SABR		Stereotactic ablative radiotherapy
SOBP		Spread-Out Bragg Peak
SSDL		Secondary Standards Dosimetry Laboratory
TCP		Tumor Control Probability

TG-51	Task Group 51
TRS-398	Technical Report Series No. 398
VMAT	Volumetric modulated arc therapy
WET	Water-equivalent thickness

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Chapter 1

Overview

1.1 Research motivation

Cancer remains a leading cause of mortality worldwide, with an estimated 20 million new cases and 9.7 million deaths in 2022 [1]. Over a lifetime, roughly one in five people will develop cancer, and about one in nine men and one in twelve women will die from it. The burden is expected to grow further as populations age and expand, and as exposure to major risk factors such as tobacco, alcohol, obesity and air pollution persists [2]. Current projections suggest that the annual number of new cases will rise to 35 million by 2050, with cancer deaths increasing to approximately 18.5 million. These projections highlight the need for advancing research in cancer prevention, early diagnosis and effective treatment strategies.

Several treatment modalities are available, the most common being surgery, radiation therapy and chemotherapy. The choice of treatment depends on multiple factors, such as tumor location and disease stage, and in many cases a combination of different methods is used. Approximately half of all cancer patients receive radiation therapy at some stage of their treatment [3].

Radiation therapy uses ionizing radiation such as photons, electrons, protons, or heavier ions to destroy cancer cells. It can be delivered externally, using medical accelerators to produce high-energy beams directed at the tumor, or internally, by placing a radioactive source close to or inside the tumor. External beam radiation therapy remains the predominant technique. The primary goal of radiotherapy is to optimize tumor control while minimizing side effects. This is achieved by maximizing the dose delivered to the tumor while minimizing the exposure of healthy tissues, through the appropriate selection of beam type, energy, and direction.

Traditionally, most patients are treated with photon beams produced by linear accelerators. However, a growing interest in particle therapy has emerged, which uses protons or light ions. These charged particles have distinct physical and biological advantages: they deposit the majority of their energy at a well-defined depth (the Bragg peak), enabling more conformal dose distributions in the tumor while sparing critical organs nearby.

The success of any radiation therapy treatment ultimately depends on the accuracy of the dose delivered. Recommendations from the International Commission on Radiation Units and Measurements (ICRU) suggest that the absorbed dose to the target should be delivered with an accuracy of about $\pm 5\%$, corresponding to one standard deviation [4]. Wambersie and colleagues later

proposed a standard uncertainty of 3.5%, while recognizing that in some scenarios larger uncertainties may be acceptable [5]. Many steps in the radiation therapy workflow contribute to the overall dose uncertainty, including dosimetry, dose calculation and optimization in treatment planning, patient positioning, and beam delivery.

Accurate dosimetry is therefore essential for safe and effective radiation therapy. While dosimetry for high-energy photon beams is well established, larger uncertainties remain for particle therapy. For protons and light ions, the determination of absorbed dose to water is associated with increased uncertainty, largely due to the limited availability of experimental data and the complexity of particle interactions in matter. In clinical practice, ionization chambers are the most widely used detectors, but they require calibration in a reference beam and the application of a beam quality correction factor, k_Q , when used in a different radiation quality. The uncertainty associated with these k_Q -factors is substantially higher in particle beams than in photon beams, reflecting both limited experimental data and modeling challenges [6].

Reducing these uncertainties requires experimental determination and validation of k_Q -factors. As a primary standard technique, water calorimetry provides a direct measurement of absorbed dose to water and is therefore ideally suited for this purpose. The objective of this work is to use water calorimetry to experimentally determine k_Q -factors for a range of ionization chambers in photon, proton, and light ion beams, and to assess their consistency with existing protocols and Monte Carlo calculations. This ultimately contributes to more accurate and reliable dosimetry for different modalities such as proton, carbon and helium ion therapy.

1.2 Main contributions

The objective of this thesis is to reduce uncertainties in reference dosimetry for particle therapy by means of water calorimetry. The work is structured around four main scientific contributions.

1.2.1 Evaluation of ionization chambers for high-energy photon reference dosimetry

Although reference dosimetry in high-energy photon beams is well established, certain ionization chamber types commonly used in clinical practice are currently not included in international dosimetry protocols. This work evaluates the suitability of these chambers as reference dosimeters in high-energy photon

beams. Beam quality correction factors were determined experimentally using water calorimetry, and chamber-specific correction factors such as polarity and recombination were assessed. In addition, the long-term stability of the chambers was evaluated. The results provide additional experimental data for these chamber types, providing additional insight into their behavior in high-energy photon beams.

1.2.2 Experimental determination of k_Q -factors in proton beams

Compared with conventional photon beams, reference dosimetry in proton therapy is associated with larger uncertainties. This increased uncertainty is dominated by the uncertainty on the beam quality correction factors, for which experimental data in proton beams is scarce. This work addresses this gap by experimentally determining beam quality correction factors for different ionization chamber types commonly used in clinical proton dosimetry, using water calorimetry. Measurements were performed at two proton therapy centers and with different calorimeter configurations, providing robust and reproducible results. The work provides experimental validation of current reference dosimetry recommendations and expands the experimental database of k_Q -factors in scanned proton beams.

1.2.3 Experimental determination of k_Q -factors in carbon and helium ion beams

Even more than for proton beams, beam quality correction factors for carbon and helium ion beams are associated with large uncertainties. For carbon ions, only a limited number of experimental data points are available and only for a small subset of ionization chamber types, while for helium ion beams no experimental data is currently available. This work addresses this gap by determining beam quality correction factors in scanned carbon and helium ion beams using water calorimetry. Measurements were performed at two independent particle therapy centers and for a range of commonly used ionization chamber types, resulting in an extensive experimental dataset of k_Q -factors for light ions. These data provide a much-needed experimental basis for the further refinement of dosimetry protocols in light ion therapy.

1.2.4 Comparison of water and graphite calorimetry in carbon ion beams

Primary standards of absorbed dose are realized using different calorimetric techniques. In this work, a direct comparison was performed between the UCLouvain water calorimeter and the National Physical Laboratory (NPL)

graphite calorimeter in carbon ion beams. This collaboration provides an important cross-validation between two independent calorimetric techniques and contributes to the metrological consistency of absorbed dose measurements in carbon ion therapy.

1.3 Thesis outline

Chapter 1 introduces the research motivation and summarizes the main scientific contributions of this thesis.

Chapter 2 introduces the background necessary to understand the work conducted in this thesis. It begins with a general overview of radiotherapy and the different treatment modalities currently in use, highlighting their respective advantages and limitations. The chapter then presents the fundamentals of dosimetry and metrological traceability, followed by an introduction to the detector types most relevant to this work. Finally, it outlines the general framework of clinical reference dosimetry, including the $N_{D,w}$ -formalism used to determine absorbed dose.

Chapter 3 provides a broad and technical overview of the water calorimeter used in this work. It describes the different components, experimental setup, operational procedures, calibration steps, and the correction factors applied to obtain accurate absorbed dose measurements.

Chapters 4-7 detail the main scientific contributions presented within this thesis.

Chapter 4 evaluates the performance of selected ionization chambers in high-energy photon beams.

Chapter 5 presents the experimental determination of k_Q -factors in scanned proton beams.

Chapter 6 reports the determination of k_Q -factors in scanned carbon and helium ion beams.

Chapter 7 describes the comparison between the water calorimeter and the NPL graphite calorimeter in carbon ion beams.

Chapter 8 discusses the overall findings of this thesis, highlights their implications for reference dosimetry in particle therapy, discusses limitations and provides perspectives for future research and protocol development.

Chapter 2

Background

2.1 Radiation therapy

Cancer arises when mutations disrupt normal cell division, allowing cells to proliferate uncontrollably and form malignant tumors. Radiation therapy treats cancer by using ionizing radiation to deposit energy within tissues, causing DNA damage either directly (bond breaks) or indirectly by producing free radicals capable of inducing single- and double-strand breaks. Complex DNA damage of this kind is difficult for cells to repair and forms the biological basis for radiation therapy.

The aim of radiotherapy is to deliver a sufficiently high dose to the tumor to cause irreversible DNA damage while minimizing exposure to surrounding healthy tissues. Achieving this balance depends on the physical properties of the radiation beam, the type and position of the tumor, the radiosensitivity of the tumor and normal tissues, and the geometrical accuracy of the treatment delivery. Even small deviations between the prescribed and delivered dose can influence both tumor control and normal tissue toxicity.

Since the first medical use of X-rays at the end of the nineteenth century [7], radiotherapy has evolved into a highly advanced and diverse treatment modality. The introduction of medical linear accelerators in the mid-twentieth century established external photon beams as the clinical standard, with electrons later added for the treatment of superficial lesions. Charged particle therapy followed, beginning with protons and later with carbon ions, and has grown steadily in

recent decades due to its favorable physical and biological characteristics [8, 9].

Today, multiple radiation modalities are available for clinical use, each with characteristic dose deposition patterns and biological effects. To understand the differences between photon, electron, and particle beams and their respective clinical advantages and limitations, it is first necessary to introduce several fundamental physical and biological concepts.

2.2 Fundamental concepts in radiation physics and biology

The physical interactions of ionizing radiation with matter determine how energy is deposited in tissue and therefore shape the resulting biological effects. These fundamental processes differ between photons, electrons, protons and light ions, leading to distinct depth-dose patterns and variations in the complexity of DNA damage they induce. This section introduces several key concepts that describe these mechanisms: the interaction of radiation with matter, absorbed dose, the notion of linear energy transfer, and the relative biological effectiveness.

2.2.1 Interaction of ionizing radiation with matter

The interaction of ionizing radiation with matter lies at the heart of radiation therapy. A fundamental distinction is made between non-charged particles, such as photons and neutrons, and charged particles, such as electrons, protons, and light ions.

Uncharged particles

Since neutrons are not used in this work, the following discussion focuses on photons, which also constitute the most widely used radiation modality in clinical radiotherapy.

Photons deposit energy in matter indirectly, through the production of secondary charged particles. When a photon beam enters a medium, its energy is transferred to atomic electrons via a number of interaction processes, after which these electrons deposit their energy through ionization and excitation. The nature and relative importance of these interaction mechanisms depend strongly on the photon energy and the atomic number Z of the absorbing material [10].

At low photon energies, elastic scattering processes may occur, in which the

incident photon is deflected with negligible energy transfer to the medium. At higher photon energies, three interaction mechanisms dominate. In the photo-electric effect, the photon is completely absorbed, and an atomic electron is ejected. In Compton scattering, the photon transfers part of its energy to an electron and is deflected with reduced energy. In pair production, which becomes significant at high energies, the photon is converted into an electron-positron pair in the presence of an atomic nucleus [11]. As a photon beam passes through matter, these interactions reduce the number of photons in the beam, resulting in a decrease in intensity. This process, known as attenuation, is described by the exponential attenuation law [12]:

$$I(x) = I_0 e^{-\mu x} \quad (2.1)$$

In this equation, $I(x)$ denotes the photon beam intensity after traversing x cm of material, while I_0 is the incident beam intensity. The parameter μ is the linear attenuation coefficient and characterizes the probability per unit path length that a photon undergoes an interaction in the medium.

In the megavoltage (MV) energy range used for radiotherapy, the dominant photon interactions are Compton scattering and pair production [13]. Both processes generate energetic secondary electrons that travel non-negligible distances (in the order of several millimeters to a few centimeters) in tissue depositing energy along their track. As a consequence, energy deposition does not occur exactly at the site of the initial photon interaction but is spatially distributed downstream. This leads to the characteristic dose build-up region near the surface, where the absorbed dose increases with depth until charged particle equilibrium is established, after which it decreases exponentially with depth, as illustrated in figure 2.1 [14].

Charged particles

Charged particles such as electrons, protons, and light ions interact with matter predominantly through electromagnetic forces. As they travel through a medium, they continuously lose energy through Coulomb interactions with atomic electrons, which leads to ionization and excitation. In addition, elastic scattering on atomic nuclei causes angular deflections of the particle trajectory and contributes to lateral beam spreading, but only weakly to the total energy loss.

The detailed nature of these interactions depends on the mass, charge, and

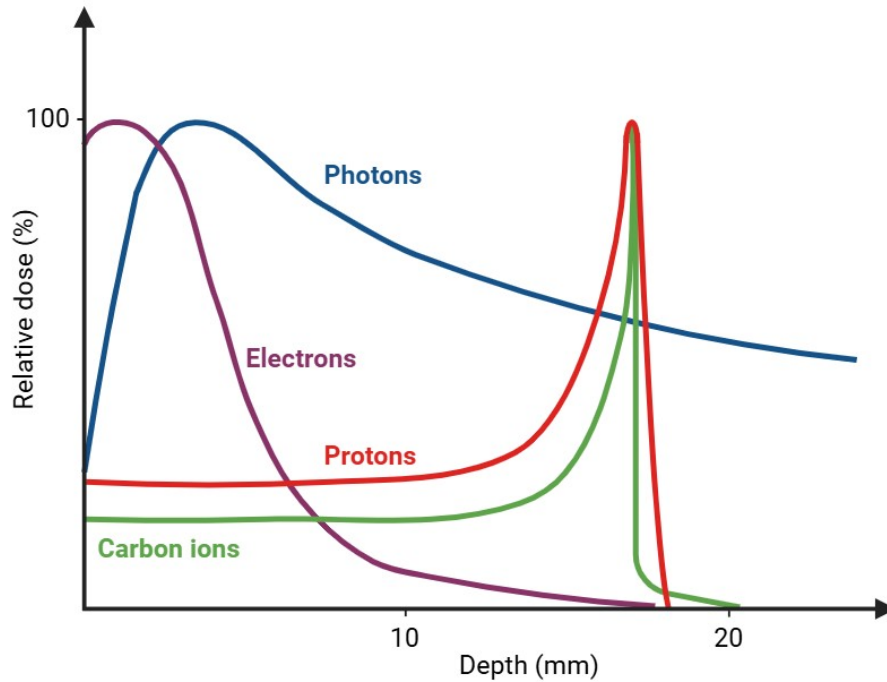


Figure 2.1: Relative dose as a function of depth for different radiation modalities used in radiotherapy. Charged particles exhibit a pronounced Bragg peak, whereas photons show an exponential dose fall-off.

energy of the incident particle. Light charged particles such as electrons have a small mass and therefore they undergo large angular deflections, resulting in variable trajectories. Their energy loss is dominated by Coulomb interactions, while radiative losses due to bremsstrahlung become significant only at higher energies and in high-Z materials. In therapeutic electron beams, energy loss due to Coulomb scattering dominates, leading to a relatively shallow penetration depth and a rapid fall-off of dose beyond the useful range [10].

Heavier charged particles, such as protons or carbon ions, interact with matter through similar Coulomb interactions but behave very differently because of their much larger mass. They experience much smaller angular deflections and therefore travel along nearly straight paths through tissue. Because charged particles lose energy continuously along their trajectory, their energy deposition pattern differs fundamentally from that of photons. The mean rate of energy loss (dE) per unit path length (dx), known as the stopping power, increases

as the particle slows down. This behavior is approximately described by the Bethe-Bloch equation [15]:

$$-\frac{dE}{dx} = \left(\frac{ze^2}{4\pi\epsilon_0} \right)^2 \frac{4\pi Z\rho N_A}{Amv^2} \left[\ln\left(\frac{2mv^2}{I} \right) - \ln(1 - \beta^2) - \beta^2 \right] \quad (2.2)$$

where $v = \beta c$ is the ion velocity and ze its electronic charge, m is the electron mass, N_A is Avogadro's number, A is the atomic mass number, Z is the atomic number, ρ is the density of the stopping material and I is the mean excitation energy.

In the energy range of clinical proton beams, the stopping power depends strongly on $1/v^2$. Consequently, protons deposit relatively little energy while traveling at high speed in the entrance region of the medium. As they penetrate deeper and slow down, the energy deposited per unit path length increases remarkably. This leads to a characteristic depth-dose profile consisting of a nearly uniform plateau region followed by a sharp maximum in dose near the end of the proton range, known as the Bragg peak. Beyond this point, the dose falls rapidly to zero because the protons have come to rest, as illustrated in figure 2.1. For light ions (such as carbon ions and helium ions), nuclear interactions along the beam path lead to fragmentation into lighter particles, which continue to deposit dose beyond the Bragg peak, forming a characteristic fragmentation tail [16].

2.2.2 Absorbed dose

The delivery of radiation without a means to quantify and measure it is meaningless. The quantity of interest is the absorbed dose, D which is defined as the mean energy (dE) imparted per unit of mass (dm) and is expressed in Gray (Gy), defined as J kg^{-1} [10]:

$$D = \frac{dE}{dm} \quad (2.3)$$

2.2.3 Linear Energy Transfer

Linear energy transfer (LET) describes the density of energy deposited by an ionizing particle along its path. It is defined as the mean energy deposited per unit path length in a given material (expressed in $\text{keV } \mu\text{m}^{-1}$). LET is closely related to the stopping power, which describes the total energy lost by the particle.

However, part of this energy may be carried away by secondary electrons, which deposit their energy at some distance from the primary track. To account for this, the concept of restricted LET (LET_Δ) is introduced, in which only the energy transferred to secondary electrons below a given cutoff energy is considered. In contrast, unrestricted LET (LET_∞) includes all energy transfers and is equivalent to the linear collision stopping power [17]. The choice between restricted and unrestricted LET depends on the spatial and biological scale of interest.

Radiation types differ substantially in their LET: photons and electrons exhibit sparse and widely spaced interactions and are classified as low-LET radiation, whereas charged particles such as carbon ions, deposit energy much more densely and are considered high-LET radiation [14].

In tissue, the way energy is deposited along the particle track plays a major role in determining the type and severity of cellular damage. High-LET radiation creates densely packed ionization events over short distances, leading to complex DNA damage that is difficult to repair. As a result, for an equal absorbed dose, high-LET radiation tends to produce stronger and more irreparable biological damage compared to low-LET radiation. This link between energy deposition and the resulting biological response forms the basis of the relative biological effectiveness concept.

2.2.4 Relative Biological Effectiveness

The relative biological effectiveness (RBE) quantifies the biological response of a given type of radiation relative to a reference radiation, typically 250 keV photons, which are assigned an RBE of 1. It is defined as the ratio of the absorbed dose of the reference radiation to the absorbed dose of the radiation under investigation required to produce the same biological endpoint. For example, if 1 Gy of a given radiation type produces the same biological effect as 2 Gy of 250 keV photons, then that radiation has an RBE of 2. RBE is strongly influenced by LET: in general, RBE increases with LET up to a peak (around $100 \text{ keV } \mu\text{m}^{-1}$), beyond which it decreases due to overkill effects [14, 18]. However, RBE is a complex quantity that depends on multiple biological and experimental factors such as cell type, dose rate, oxygenation and more. Because of this complexity, RBE values represent simplified approximations rather than universal biological constants.

2.3 Treatment modalities in radiotherapy

Having introduced the fundamental principles that govern how radiation deposits energy in matter, we can now consider how these concepts translate to clinical practice. Modern radiation therapy makes use of several distinct modalities, including photons, electrons, protons, helium ions, and carbon ions. Each modality not only differs in terms of its physical dose distribution and biological effectiveness, but also in its technological complexity, clinical applications, and associated costs. A clear understanding of these differences is crucial to appreciate why certain modalities are chosen for specific treatments and how emerging particle therapies aim to improve the balance between tumor control and normal-tissue preservation. The following sections provide an overview of the main characteristics, advantages, and limitations of the main radiation types employed or under development in clinical radiotherapy.

2.3.1 Cobalt-60

Cobalt-60 (^{60}Co) radioactive sources were historically used for external beam radiotherapy and emit photons at discrete energies of 1.17 MeV and 1.33 MeV through radioactive decay [19]. Although largely replaced in clinical practice, ^{60}Co remains of importance in radiation dosimetry [6]. Owing to its stable and well-defined photon spectrum, it is widely used as a reference radiation for the calibration of ionization chambers and dosimetric systems, and will therefore reappear as a key reference beam in the later chapters of this thesis.

2.3.2 Photons

Photon therapy is the most widely used form of external beam radiotherapy and relies on high-energy photons to deliver dose to tumors. Modern linear accelerators can generate megavoltage photon beams with well-characterized depth-dose profiles, often combined with advanced imaging modalities such as cone-beam CT or MRI-guided systems to improve treatment accuracy [20]. Owing to decades of technological development, photon therapy is highly accessible worldwide and remains the clinical standard for the majority of cancer treatments. One of its major strengths is its versatility: photons can be shaped and modulated using techniques such as intensity-modulated radiotherapy (IMRT), volumetric-modulated arc therapy (VMAT), and stereotactic ablative radiotherapy (SABR), enabling conformal tumor coverage across a broad range of anatomical sites [21–23].

However, photons are low-LET radiation and deposit dose along their entire

path through the patient. As a result, healthy tissues both proximal and distal to the tumor receive non-negligible radiation exposure. This can lead to significant acute and late toxicities, and contributes to an increased risk of radiation-induced secondary cancers, especially in younger patients [24]. Despite these limitations, the combination of widespread availability, robust dose delivery, and mature clinical infrastructure makes photon therapy the backbone of modern radiotherapy.

2.3.3 Electrons

Electron therapy uses high-energy electron beams, generated by clinical linear accelerators, to treat superficial tumors. Owing to their limited penetration depth and rapid dose fall-off, electrons are well suited for lesions close to the surface [25]. As low-LET radiation, their biological effectiveness is similar to that of photons [26]. However, because their range is restricted to only a few centimeters, electrons play a limited role in modern radiotherapy and are included here only for completeness, as they are not part of this work.

2.3.4 Protons

Proton therapy uses accelerated protons to deliver highly localized radiation doses to tumors. Owing to their characteristic depth-dose profile, protons exhibit a pronounced Bragg peak with a steep distal fall-off, enabling improved sparing of surrounding healthy tissues compared with photon or electron beams.

In clinical practice, protons are typically accelerated using a cyclotron or synchrotron to maximum energies of up to approximately 250 MeV, with the selected beam energy determined by the depth of the target volume [27]. Higher energies are required to reach deeper-seated tumors, whereas lower energy beams, on the order of 70 MeV, are sufficient for shallow targets. A monoenergetic proton beam produces a single, well-defined Bragg peak, which is suitable for treating small lesions at a specific depth. However, most clinical tumors extend over a finite volume, making a single Bragg peak insufficient for uniform target coverage. To address this, the proton beam energy is modulated so that multiple Bragg peaks at different depths are superimposed, forming a spread-out Bragg peak (SOBP) that delivers a nearly uniform dose across the tumor volume while preserving the sharp distal dose fall-off (figure 2.2). This depth–dose shaping is a central feature of proton therapy and underpins its dosimetric advantages, including reduced integral dose to healthy tissue compared to photon beams. In practice, the magnitude of these benefits depends on factors such as tumor site, treatment geometry, and uncertainties related to

patient anatomy and motion.

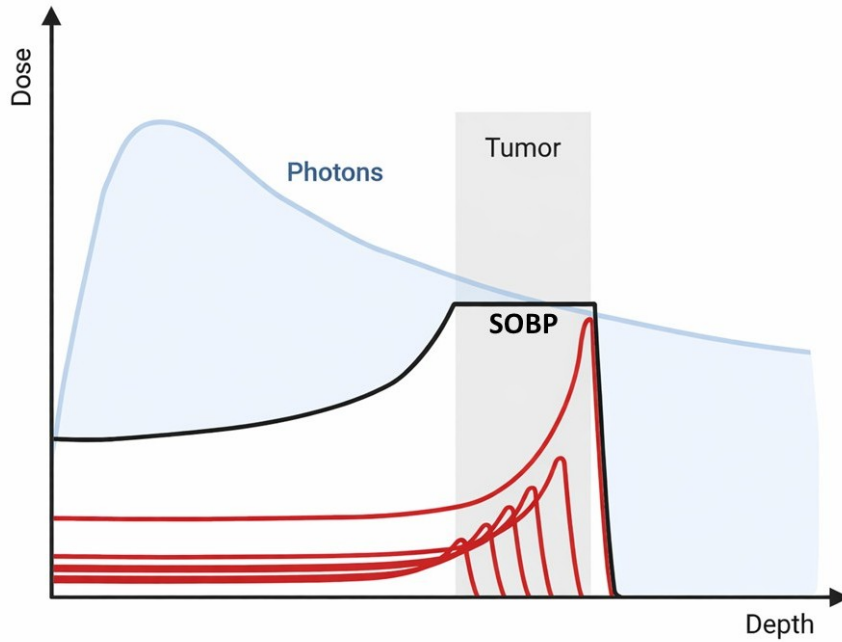


Figure 2.2: Depth-dose curves illustrating the difference between photon and proton therapy. Photon beams deposit dose along their entire path through the patient, resulting in entrance and exit dose beyond the tumor volume. In proton therapy, multiple monoenergetic Bragg peaks of different energies are superimposed to form a Spread-Out Bragg Peak (SOBP), providing a nearly uniform dose across the tumor while maintaining a sharp distal fall-off. Adapted from [28].

Two principal techniques have been developed to shape and deliver proton beams clinically [9]. Historically, passive scattering methods were the first to be widely implemented. In this approach, the initially narrow proton beam is broadened laterally using scattering foils, while a SOBP is created in depth using range modulators such as rotating modulator wheels or ridge filters. Although passive scattering allows for rapid dose delivery, it requires patient-specific hardware, offers limited proximal dose conformity, and produces additional neutron radiation due to interactions with beam-modifying components. As a result, its use has declined in favor of more advanced delivery techniques. Modern proton therapy centers predominantly employ active scanning methods, most notably pencil beam scanning (PBS) [29–31]. In PBS, narrow proton

beamlets are magnetically steered across the target volume to achieve lateral dose shaping, while depth modulation is accomplished by varying the beam energy to deliver a sequence of discrete energy layers. This spot-by-spot and layer-by-layer delivery enables highly conformal dose distributions and improved sparing of organs at risk. However, scanning techniques are generally slower than passive methods, as the beam energy must be changed between layers, introducing additional delivery time.

From a radiobiological perspective, protons are considered low-LET particles, and their biological effectiveness is therefore similar to that of photons. In clinical proton therapy, a constant relative biological effectiveness value of 1.1 is commonly assumed, despite known variations with depth and LET [32]. Clinically, proton therapy is particularly advantageous in scenarios where normal-tissue sparing is critical, such as pediatric treatments, head-and-neck and skull-base tumors [33–35]. Although the number of proton therapy centers has increased steadily and currently exceeds one hundred worldwide [36], proton therapy remains considerably more expensive than conventional photon therapy. This is primarily due to the need for large-scale accelerator systems, such as cyclotrons or synchrotrons, which require substantial space and investment compared to the linear accelerators used for photon beams [27].

2.3.5 Light ions beams

Light ions heavier than protons, such as carbon and helium ion beams have been investigated for use in radiotherapy due to their distinct physical and biological properties, which offer potential clinical benefits but also introduce their own additional challenges [37].

Carbon ions

Carbon ions are currently the only light ion beams routinely used in clinical practice. Carbon ion therapy is an advanced form of external beam radiotherapy, combining highly favorable physical dose distributions with a markedly increased biological effectiveness. Due to their higher mass and charge, carbon ions exhibit minimal lateral scattering and produce an extremely sharp Bragg peak, enabling highly conformal dose delivery and potential effective sparing of surrounding healthy tissue [38]. In clinical practice, ripple filters are used to broaden the Bragg peak, thereby achieving a more uniform dose distribution over the target volume. A key feature of carbon ions is their high linear energy transfer, which increases substantially towards the Bragg peak region. This results in dense ionization tracks and complex DNA damage, leading to an elevated

RBE [39]. This increased RBE may provide clinical advantages for the treatment of radioresistant or hypoxic tumor cells compared to low-LET radiation [40].

Despite these potential advantages, the widespread adoption of carbon ion therapy remains limited. Carbon ion facilities require large, complex and expensive accelerator infrastructures, typically based on synchrotrons, resulting in high construction and operational costs [27]. In addition, treatment planning is more challenging than for photon and proton therapy due to the depth-dependent RBE and the need for sophisticated biological models. As of December 2025, 16 carbon ion therapy facilities are in operation worldwide, with additional centers currently under construction or in the planning phase [36].

Helium ions

Although helium ions were investigated in early radiotherapy research [41], clinical interest has re-emerged only recently due to advances in accelerator technology and renewed appreciation of their favorable physical properties [42]. At present, helium ion therapy is available only at a limited number of research-oriented facilities and has not yet been adopted for routine clinical use, although clinical treatments have recently been initiated at the Heidelberg Ion Beam Therapy Center (HIT) [43, 44]. Nevertheless, helium ions are increasingly regarded as a promising modality as they occupy an intermediate position between proton and carbon ion therapy in terms of both physical and biological properties. Compared with protons, helium ions exhibit reduced lateral scattering, resulting in a narrower lateral penumbra and improved dose conformity, while maintaining a well-defined Bragg peak [42, 45–47]. Although helium ions also exhibit a fragmentation tail beyond the Bragg peak, this is smaller than for carbon ions. Their LET, and consequently their RBE, is moderately higher than that of protons but substantially lower than that of carbon ions, offering a potentially favorable balance between physical precision and biological effectiveness [48, 49]. From a technical perspective, helium ions also present several potential advantages over carbon ions. Their production may be feasible using cyclotron-based accelerator systems, which are generally less complex and less costly than the synchrotrons required for carbon ion therapy [27].

While these treatment modalities differ in their physical and biological characteristics, the clinical relevance of these differences ultimately depends on the relationship between delivered dose and treatment outcome. In external beam radiotherapy, the radiation used to treat a tumor inevitably also affects the surrounding healthy tissues. As a result, the DNA in healthy tissues may also be damaged. However, healthy cells generally retain a greater capacity for repair than tumor cells, whose repair mechanisms are often impaired. This difference gives rise to what is known as the therapeutic window. The objective of treatment is therefore to deliver a sufficiently high dose to achieve tumor control, while minimizing the risk of damage to normal tissues. This balance is commonly described using the concepts of tumor control probability (TCP) and normal tissue complication probability (NTCP), which are typically represented as sigmoidal dose-response curves (figure 2.3) [50]. In the clinically relevant dose range, these curves can be steep, meaning that relatively small deviations in the delivered dose can lead to significant changes in tumor control or normal tissue toxicity. This strong sensitivity to dose underlies the stringent accuracy requirements in radiotherapy, where the overall uncertainty in absorbed dose is generally recommended to remain below 5% [4].

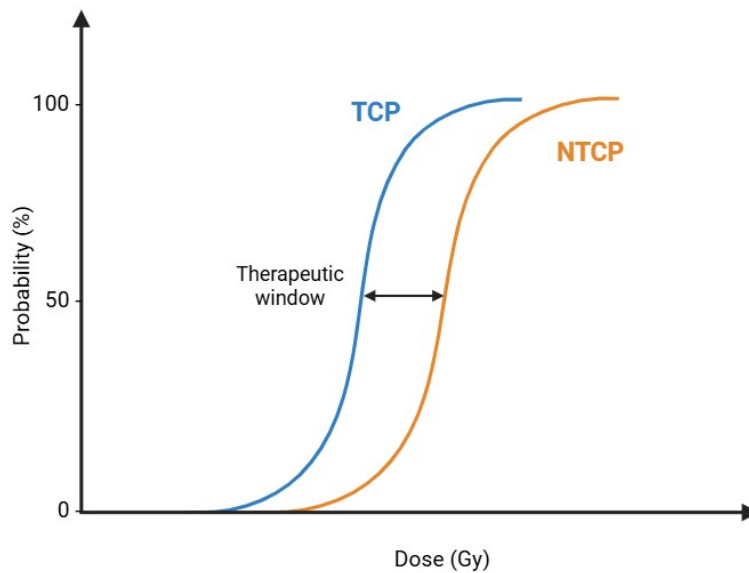


Figure 2.3: Schematic representation of tumor control probability (TCP) and normal tissue complication probability (NTCP) as a function of absorbed dose. The region between the two curves represents the therapeutic window. Adapted from [51].

2.4 Dosimetry

The accurate delivery of a prescribed dose to the target volume is crucial to achieve tumor control while minimizing damage to the surrounding healthy tissue. Achieving this requires a reliable and traceable dosimetry chain, enabling the dose delivered to be measured with high accuracy. As introduced before, the quantity of interest is absorbed dose, expressed in Gray. Since human tissues are largely composed of water, absorbed dose to water, D_w , is used as the reference quantity in clinical dosimetry. To ensure that dose measurements in individual clinics are accurate and comparable, a hierarchical system of standards is used (figure 2.4). At the top of this hierarchy are primary standards, which establish the absorbed dose at the national and international level. This is then disseminated to secondary standards, and, ultimately, to the clinical users through calibrated dosimeters. This chain of traceability forms the foundation of all dose measurements in radiation therapy.

2.4.1 Primary standards

Primary standards of absorbed dose are instruments or methods that determine the absorbed dose directly from fundamental physical principles, without requiring calibration against another radiation measurement device. They define the absorbed dose scale at national and international level and form the foundation of the entire dosimetry traceability chain. Although primary standards do not require calibration in terms of radiation dose, they may rely on calibrations of other physical quantities (e.g., electrical power or temperature), but no external radiation measurement enters the determination of dose.

Primary standards must operate at the highest metrological level available, with uncertainties comparable to the best achievable in the field. They are typically realized and maintained by Primary Standards Dosimetry Laboratories (PSDLs), such as the National Physical Laboratory (NPL, Teddington, UK) or the Physikalisch-Technische Bundesanstalt (PTB, Braunschweig, Germany). To ensure international consistency of absorbed dose scales, these standards are regularly compared. Such international comparisons provide essential validation and demonstrate the accuracy and equivalence of national standards on a global scale [52, 53].

Several methods can serve as primary standards for absorbed dose. Three main categories exist: calorimetry, chemical dosimetry and ionization-based standards [55]. Among these, calorimetry is the most widely used approach in PSDLs [10]. As this thesis focuses on water calorimetry and ionization chamber

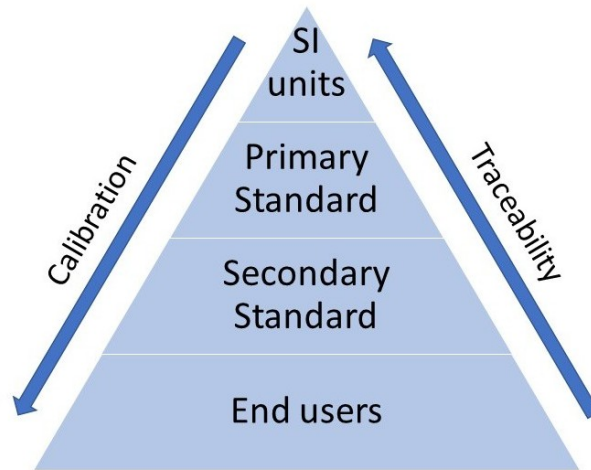


Figure 2.4: Schematic representation of the traceability chain for absorbed dose measurements in radiotherapy. Primary standards establish the absorbed dose scale in terms of SI units, which is disseminated to secondary standards and ultimately to clinical end users through calibrations. The upward arrow indicates traceability to SI units, while the downward arrow represents calibration transfer. Adapted from [54].

measurements, only calorimeters and the relevant ionization chamber concepts are discussed in detail in sections 2.5.1 and 2.5.2.

2.4.2 Secondary standards

Secondary standards play a key role in transferring absorbed dose measurements from primary standards to clinical and research users. This transfer is achieved through the calibration of secondary standard dosimeters against primary standards, after which the secondary standards are used to calibrate user instruments. In this way, user dosimeters are traceable to a primary standard. The international framework for this traceability chain is coordinated by the Bureau International des Poids et Mesures (BIPM) and implemented through Secondary Standards Dosimetry Laboratories (SSDLs). Secondary standards are well established and should exhibit good long-term stability. Ionization chambers are the detectors of choice for this purpose. The principal role of SSDLs is to bridge the gap between PSDLs and users of ionizing radiation by enabling the reliable dissemination of absorbed dose calibrations.

2.4.3 Absolute, reference and relative dosimetry

In radiation dosimetry, a distinction is commonly made between absolute, reference, and relative dosimetry. Absolute dosimetry refers to the determination of the quantity of interest directly from fundamental physical principles using a primary measurement standard. Reference dosimetry is performed at the user's facility using a detector that has been calibrated at a standards laboratory, most commonly ionization chambers. Measurements are carried out under well-defined reference conditions at a reference point on the beam central axis and at a well defined reference depth z in water. Additional parameters, such as field size and source-to-surface distance, are also specified. These reference conditions and procedures are defined in international dosimetry protocols, such as the IAEA TRS-398 Code of Practice, which ensure consistency and comparability of absorbed dose measurements between institutions [6]. Relative dosimetry refers to measurements performed under non-reference conditions in the user beam and is typically used to characterize dose distributions, beam profiles, and depth-dose variations, using different types of detectors.

2.5 Detectors

A wide range of detectors is used in radiation dosimetry, each with their own advantages and disadvantages. In this thesis, the focus is on water calorimetry and ionization chambers, and only these detector types are therefore discussed in detail. A general overview of the principles of calorimetric detectors is provided in the following section, while a more technical and detailed description of the water calorimeter used in this work is presented in chapter 3.

2.5.1 Calorimeters

Calorimetry provides one of the most direct methods for determining absorbed dose, as the energy deposited in the absorbing material appears directly as heat. A calorimeter therefore determines absorbed dose by measuring the irradiation-induced temperature rise in a well-defined mass of material. According to the fundamental relation:

$$D_m = c_m \cdot \Delta T, \quad (2.4)$$

the absorbed dose is obtained by multiplying the temperature rise ΔT by the specific heat capacity of the medium c_m . Although this principle is conceptually simple, practical realizations require a series of corrections. Temperature

sensors perturb the system, heat may leak between the calorimeter core and its surroundings, and impurities can introduce chemical effects. To account for these influences, corrections are added based on detailed modeling.

Two types of calorimeters are commonly employed as primary standards: graphite calorimeters and water calorimeters, each with distinct advantages and challenges.

Graphite calorimeters

Graphite is often chosen as calorimetric medium due to its excellent thermal properties, chemical stability, and radiation interaction characteristics that closely resemble those of water. Its solid form enables the construction of a geometrically stable and well-defined calorimeter core containing one or more temperature sensors and electrical heating resistors. The specific heat capacity of graphite is approximately $700 \text{ J kg}^{-1} \text{ K}^{-1}$ at room temperature [56]. Figure 2.5a shows a highly simplified schematic of a graphite calorimeter, based on the design of Domen and Lamperti [57], which forms the basis of many graphite calorimeters used worldwide. It consists of a graphite core containing one or more temperature sensors surrounded by several graphite layers, referred to as jackets, which are separated by vacuum gaps to minimize heat exchange with the surroundings [58].

Graphite calorimeters can be operated in two modes: quasi-adiabatic and isothermal. In quasi-adiabatic mode, the temperature rise of the core is measured directly, while in isothermal mode, an electrical heating power maintains thermal equilibrium. During irradiation, the electrical power is reduced to maintain equilibrium, and this reduction directly represents the deposited energy.

Graphite calorimeters can achieve standard uncertainties in the absorbed dose to graphite below 0.2%. However, their main limitation is that clinical dosimetry requires absorbed dose to water. A conversion from dose to graphite to dose to water is therefore required, introducing additional uncertainties. This conversion can be performed in several ways, for example by applying the photon fluence scaling theorem, experimentally using transfer ionization chambers, or, more commonly today, by means of Monte Carlo simulations [58–64]. Applying this conversion, an overall standard uncertainty on the absorbed dose to water of approximately 0.3–0.5% can be achieved [10, 65, 66].

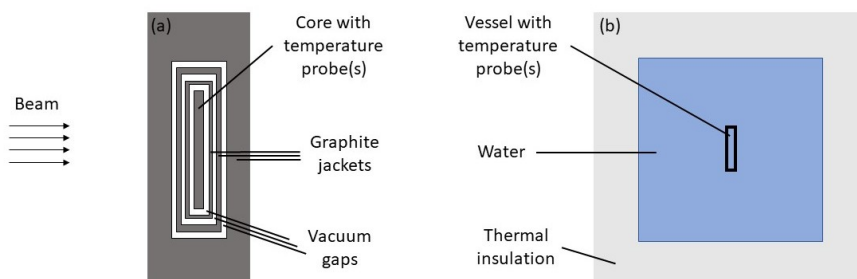


Figure 2.5: Simplified schematic of the concept of (a) a graphite calorimeter and (b) a water calorimeter.

Water calorimeters

Water calorimeters have a key conceptual advantage: they measure absorbed dose directly in water, eliminating the need for a conversion factor. However, water calorimetry presents its own challenges. The specific heat capacity of water is relatively high, approximately $4200 \text{ J kg}^{-1} \text{ K}^{-1}$ at an operating temperature of 4°C , which is approximately six times larger than that of graphite. As a result, the radiation-induced temperature rise is typically in the order of 0.24 mK Gy^{-1} , making water calorimeters inherently less sensitive than graphite calorimeters. In addition, strict control of water purity is essential, as even trace impurities can participate in radiation-induced chemical reactions that either release or absorb energy, giving rise to the so-called heat defect (see section 3.3.3). To mitigate this, the temperature sensors are enclosed within a vessel that allows the chemical composition of the surrounding water to be carefully controlled. The presence of non-water materials, such as the vessel, inevitably perturbs the measurement and must therefore be accounted for. A simplified representation of the concept of a water calorimeter is shown in figure 2.5b, based on the design of Domen [67]. Despite these challenges, modern water calorimeters can achieve standard uncertainties below 0.5%, comparable to those of graphite calorimeters [10, 68].

2.5.2 Ionization chambers

While calorimeters are essential for establishing primary standards, they are not practical for routine use in clinical settings. Instead, ionization chambers are employed as secondary standards and field instruments due to their robustness, reproducibility, and ease of use. Figure 2.6 shows a simplified representation

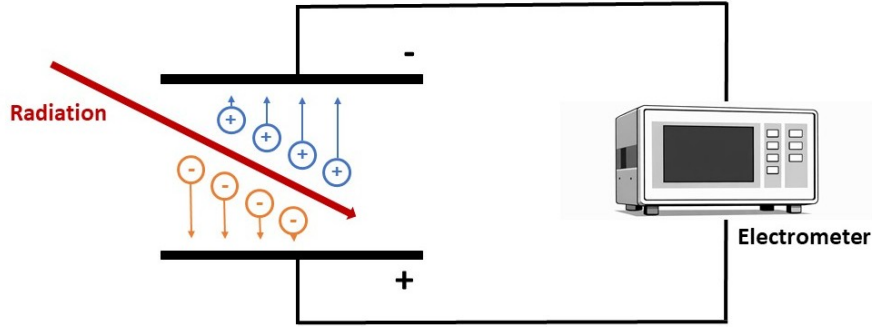


Figure 2.6: Simplified schematic of the principle of an ionization chamber. Adapted from [69].

of the concept of an ionization chamber. An ionization chamber consists of an anode and a cathode separated by an air-filled cavity across which an operating voltage is applied. When incident radiation interacts with the air in the cavity, positive and negative ion pairs are produced. Under the influence of the applied electric field, these charges drift towards the electrodes and are collected. The collected charge, measured by an electrometer, constitutes the ionization chamber signal, which can be related to absorbed dose through appropriate calibration coefficients and correction factors.

2.6 The $N_{D,w}$ -formalism

Based on international dosimetry protocols such as the International Atomic Energy Agency (IAEA) Technical Report Series n. 398 (TRS-398) [6] and the American Association of Physicists in Medicine (AAPM) Task Group 51 (TG-51) [70] Codes of Practice (CoP), the $N_{D,w}$ -formalism is used to determine the absorbed dose to water in external beam radiotherapy. This formalism is based on the use of ionization chambers calibrated in terms of absorbed dose to water, providing a direct and traceable link between primary or secondary standards and clinical dose measurements.

In this approach, an ionization chamber is calibrated by a standards laboratory, yielding a calibration coefficient $N_{D,w}$ that relates the reading of an ionization chamber to absorbed dose to water [55, 71–73]. In the ideal case, the ionization chamber is calibrated in a beam with the same radiation quality Q as that of

the user beam. Under these conditions, the absorbed dose to water in a beam of quality Q is obtained from the following relation:

$$D_{w,Q} = M_Q N_{D,w,Q} \quad (2.5)$$

where M_Q is the corrected ionization chamber reading and $N_{D,w,Q}$ is the calibration coefficient obtained in the same beam quality Q as the user beam.

In practice, however, most ionization chambers are calibrated in a reference beam of quality Q_0 , since calibrations by Primary or Secondary Standards Dosimetry Laboratories are not available for all radiation qualities. A calibration coefficient N_{D,w,Q_0} is obtained for this reference beam, and the absorbed dose to water in the user beam of quality Q is given by:

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0} \quad (2.6)$$

where k_{Q,Q_0} is the beam quality correction factor, which accounts for the difference in beam quality between the reference beam of quality Q_0 and the user beam of quality Q .

2.6.1 The corrected chamber reading M_Q

Calibration coefficients for ionization chambers are only valid under the reference conditions at which the calibration is performed. When an ionization chamber is used in a user beam, deviations from these reference conditions must therefore be corrected by applying appropriate correction factors. Assuming that the influence quantities act independently, the corrected chamber reading M_Q is obtained from the raw reading M_{raw} as

$$M_Q = M_{raw} \prod_i k_i \quad (2.7)$$

The most relevant influence quantities considered here are air density (temperature and pressure), polarity effects, and ion recombination.

Temperature and pressure

The mass of air in the ionization chamber depends on the ambient temperature and pressure, which affects the number of ion pairs produced. To account for

atmospheric variations, a temperature and pressure correction factor is applied:

$$k_{tp} = \frac{(273.15 + T)}{(273.15 + T_0)} \frac{P_0}{P} \quad (2.8)$$

where T and P are the ambient temperature and pressure at the time of measurement, and T_0 and P_0 are the corresponding reference values used during calibration (generally 20 °C and 1013.25 hPa, respectively).

Polarity

The response of an ionization chamber may depend on the sign of the applied polarizing voltage, giving rise to a polarity effect. The following correction factor:

$$k_{pol} = \frac{|M_+| + |M_-|}{2|M|} \quad (2.9)$$

is applied to take this into account. In this equation, M_+ and M_- are the chamber readings obtained at positive and negative polarity, and M is the chamber reading at the calibration polarity.

Recombination

Not all charges created in the ionization chamber are necessarily collected at the electrodes, as some of the ion pairs may recombine before collection. This incomplete charge collection, known as the recombination effect, is corrected for by applying the ion recombination correction factor k_s . Recombination may occur between ions produced along the same particle track (initial recombination) or between ions originating from different tracks (general recombination). The magnitude of recombination depends on the ionization chamber geometry, the applied polarizing voltage, and the characteristics of the radiation beam. Consequently, different correction approaches are recommended depending on the beam type.

A distinction is commonly made between pulsed and continuous radiation beams. The ion recombination correction factor can be estimated using the two-voltage method, in which the chamber reading is measured at two different voltages. Depending on the beam type, the recombination correction factor k_s can be approximated by the following expressions:

$$k_s = a_0 + a_1 \left(\frac{M_1}{M_2} \right) + a_2 \left(\frac{M_1}{M_2} \right)^2 \quad (\text{pulsed beams}) \quad (2.10a)$$

$$k_s = \frac{n^2 - 1}{n^2 - M_1/M_2} \quad (\text{continuous beams}) \quad (2.10b)$$

Here, a_0 , a_1 , and a_2 are constants tabulated in IAEA TRS-398 Rev. 1 [6], M_1 and M_2 the chamber readings obtained at the two applied voltages V_1 and V_2 , respectively, and n denotes the ratio of the two voltages (V_1/V_2).

The approximation for pulsed beams (equation 2.10a) is only valid if a plot of $1/M$ as a function of $1/V$ exhibits a linear dependence, whereas for continuous beams (equation 2.10b), linearity is expected in a plot of $1/M$ versus $1/V^2$. It should also be noted that these expressions describe general recombination only. If initial recombination is not negligible, deviations from linearity may occur and a more general approach is required, such as the formalism proposed by De Almeida and Niatel [74]. In this approach, the two-voltage method is applied over a range of instantaneous dose rates. By plotting the ratio M_1/M_2 as function of M_1 , a linear relationship is obtained, where the slope corresponds to b_1 and the intercept to $1 + b_0$. The total recombination correction is then given by:

$$k_s = 1 + \frac{b_0}{n-1} + \frac{b_1}{n-1} M_1 \quad (\text{pulsed beams}) \quad (2.11a)$$

$$k_s = 1 + \frac{b_0}{n-1} + \frac{b_1}{n^2-1} M_1 \quad (\text{continuous beams}) \quad (2.11b)$$

2.6.2 The beam quality correction factor k_{Q,Q_0}

The beam quality correction factor, k_{Q,Q_0} accounts for the differences in beam qualities and is defined as the ratio of the ionization chamber calibration coefficients at beam qualities Q and Q_0 :

$$k_{Q,Q_0} = \frac{N_{D,w,Q}}{N_{D,w,Q_0}} = \frac{D_{w,Q}/M_Q}{D_{w,Q_0}/M_{Q_0}} \quad (2.12)$$

In most cases, the reference beam quality used for calibration is that of a ^{60}Co radiation source. In this case, the beam quality correction factor is commonly

denoted as k_Q . In certain cases, high-energy photon or electron beams are used as a reference beam and in this case the more general notation k_{Q,Q_0} is used.

Several approaches are currently used to determine beam quality correction factors. The preferred method is experimental determination. Ideally, the k_Q -factor should be measured experimentally for each ionization chamber in a beam of the same quality as the user beam. In practice, this is rarely feasible due to the limited range of beam qualities available in most standards laboratories. As a result, generic experimental k_Q values, specific to a given ionization chamber type, are often used. These values are typically obtained from calorimetric measurements performed at standards laboratories, however, they do not account for chamber-to-chamber variability.

Alternative approaches include Monte Carlo-based calculations and calculations based on the following equation:

$$k_{Q,Q_0} = \frac{(s_{w,air})_Q (W_{air})_Q p_Q}{(s_{w,air})_{Q_0} (W_{air})_{Q_0} p_{Q_0}} \quad (2.13)$$

In this equation, $s_{w,air}$ is the Spencer-Attix water-to-air stopping power ratio, W_{air} the mean energy expended in air per ion pair formed, and p , the ionization chamber perturbation factor, for beam qualities Q and Q_0 . Values for $s_{w,air}$ are typically derived from Monte Carlo calculations based on stopping-power data from ICRU Report 90, which provides key data for ionization radiation dosimetry, whereas W_{air} values are typically taken directly from the report [75]. The factor p_Q accounts for the perturbation effects arising from the presence of the ionization chamber in the radiation field. These chamber-type-specific perturbation factors can be obtained from experimental measurements or Monte Carlo simulations, or are assumed to be unity when no data is available. The availability of perturbation data strongly depends on the radiation type. In practice, the product of the stopping-power ratio $s_{w,air}$ and the perturbation factor p is often determined using Monte Carlo techniques. This product, commonly denoted as f_Q is calculated as follows [76]:

$$f_Q = \left[\frac{D_w(P)}{\overline{D}_{ch-air}} \right]_Q \quad (2.14)$$

where $\overline{D}_{ch-air}$ denotes the mean absorbed dose to air in the chamber cavity and $D_w(P)$ is the absorbed dose to water at a point P . This approach is widely used

in Monte Carlo calculations of beam quality correction factors. Substituting this expression into equation 2.13 yields the following definition:

$$k_{Q,Q_0} = \frac{f_Q (W_{\text{air}})_Q}{f_{Q_0} (W_{\text{air}})_{Q_0}} \quad (2.15)$$

Generic k_Q -factors for different radiation types and ionization chamber types are provided in the IAEA TRS-398 Rev. 1 CoP, based on the approaches described above. Depending on the radiation type, the availability of experimental and calculated data varies considerably, which is also reflected in the associated uncertainties. In the following, a brief overview is given of the different radiation types and the corresponding availability of k_Q data. For a more comprehensive discussion, the reader is referred to the TRS-398 Rev. 1 CoP [6].

All k_Q values reported in TRS-398 Rev. 1 are based on Cobalt-60 as the reference beam quality. The f_{Q_0} values were determined for different chamber types using Monte Carlo data supplied by different groups [77]. For high-energy photon beams, a substantial amount of experimental and Monte Carlo data is available for a wide range of ionization chamber types and beam qualities, reflecting the extensive clinical use of this modality worldwide. The available data were contributed by multiple independent groups and standards laboratories [78–82], and the W_{air} value is the same as that for Cobalt-60, simplifying equation 2.13. Based on this comprehensive dataset, an overall standard uncertainty of approximately 0.6% is assigned to the k_Q -factors for high-energy photon beams. In contrast, the availability of k_Q data for proton beams is substantially more limited than for photon beams, owing to their more recent clinical adoption and the restricted access to suitable proton beam qualities. While a number of Monte Carlo studies have been performed [83–89], experimental determinations remain scarce [90–97], leading to a higher standard uncertainty of about 1.4%. For light ion beams, such as helium and carbon ions, the situation is even more challenging. Both experimental and Monte Carlo data are currently very limited due to the relatively recent introduction of these treatment modalities [98–103]. Consequently, the k_Q -factors for light ions recommended in TRS-398 Rev. 1 are based on equation 2.13 and have an associated standard uncertainty of approximately 2.4%.

The uncertainties associated with the k_Q -factors for proton and light ion beams constitute a substantial contribution to the overall uncertainty on the dose delivered to patients, which is recommended to remain below 5% [4, 104]. Reducing the uncertainty associated with these correction factors is therefore

essential to ensure accurate dose delivery and, consequently, optimal treatment outcomes in particle therapy. This thesis addresses this need through the experimental determination of k_Q -factors in photon, proton, carbon and helium ion beams using water calorimetry.

Chapter 3

Water calorimetry

The principle of water calorimetry is already briefly explained in section 2.5.1: by measuring the irradiation-induced temperature rise, we can determine absorbed dose to water. In this chapter, a more detailed and technical description of the water calorimeter, its operation, and the applied corrections is given. The water calorimeter used in this work follows the design of the calorimeter developed at McGill University, and detailed descriptions can also be found in the works of Sarfehnia [105] and Renaud [106].

Some elements of this chapter will necessarily overlap with the materials and methods presented in the subsequent experimental chapters. However, for completeness and clarity, all aspects related to the calorimeter design, operation, and corrections are presented together in this chapter.

3.1 The water calorimeter setup

Figure 3.1 shows a schematic overview of the setup needed to perform the water calorimeter measurements, including the different components and electrical connections. In what follows, the different components will be discussed in more detail.

3.1.1 The water calorimeter

A schematic overview of the water calorimeter is shown in figure 3.2, while a picture of the setup is shown in figure 3.3. It consists of a 30 cm × 30 cm × 30 cm water tank made out of poly(methyl methacrylate) (PMMA), which is thermally insulated by multiple layers of expanded polystyrene to minimize external temperature influences. Copper plates embedded between the insulation layers and a copper heat exchanger inside the water tank are both connected to an external refrigerator, controlling the water temperature of the calorimeter. During operation, the calorimeter is maintained at a temperature of 4 °C to avoid convection. The heat exchanger is connected to the refrigerator via a controllable valve. During the measurements, this valve is closed for the calorimeter to reach true thermal equilibrium. Three Resistance Temperature Detector (RTD) probes are used to constantly monitor the overall water temperature of the water calorimeter. Two are immersed in the water tank, and the third is positioned between the copper plate and polystyrene. The calorimeter is configured for horizontal beams and features a 1 mm thick PMMA entrance window. A magnetic stirrer at the bottom of the tank is used to mix the water and dissipate any accumulated thermal gradients when needed.

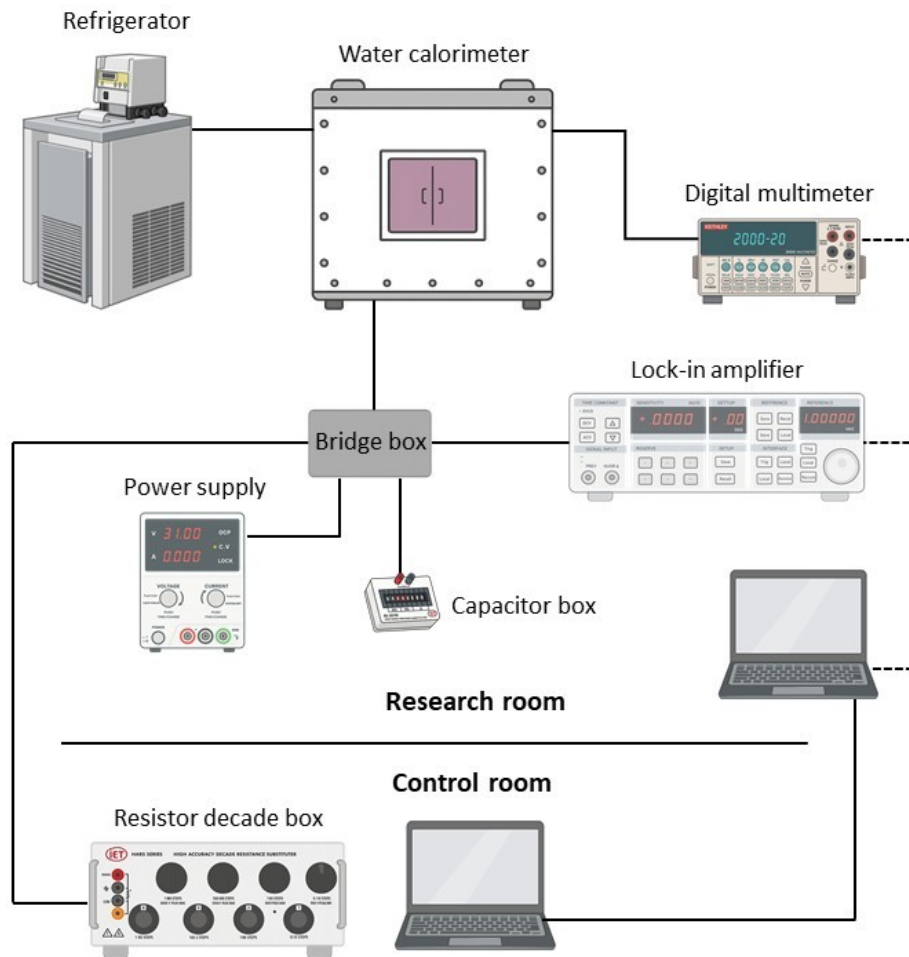


Figure 3.1: Schematic overview of the experimental setup. All major components and electrical connections are shown. The water calorimeter is connected to a refrigerator to control the bulk water temperature. Three RTD probes monitor the overall water temperature, with their signals read out using a digital multimeter. The temperature rise induced by the irradiation is measured by thermistors using an AC bridge circuit coupled to a lock-in amplifier. Both the digital multimeter and the lock-in amplifier are connected via GPIB interfaces to a laptop located in the research room for data acquisition. This laptop is remotely operated from a second laptop in the control room. A resistor decade box, located in the control room, is used to balance the AC bridge.

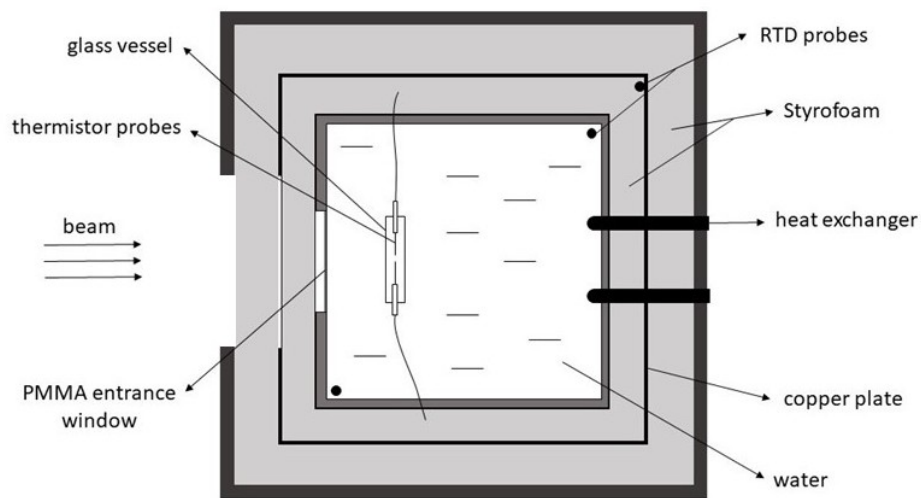


Figure 3.2: Schematic overview of the water calorimeter and its different components. The calorimeter consists of a PMMA water tank with a 1 mm thick PMMA entrance window. It is surrounded by layers of expanded polystyrene to ensure thermal insulation. A heat exchanger is positioned in the water tank to control the overall water temperature and three RTD probes are positioned inside the calorimeter to monitor this overall temperature. The plane-parallel vessel containing the two thermistor probes is positioned inside the water volume.

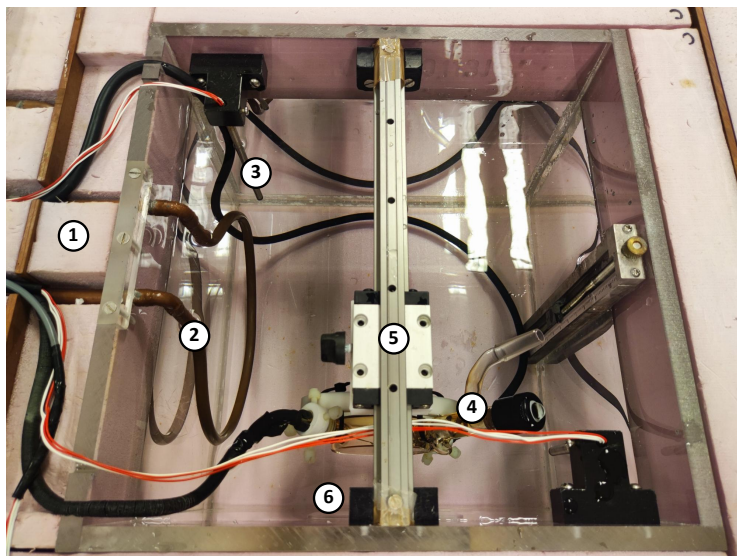


Figure 3.3: Picture of the inside of the water calorimeter showing its main components: (1) Expanded polystyrene for thermal insulation (2) heat exchanger, (3) RTD probe, (4) plane-parallel glass vessel (5) positioning bar, and (6) PMMA entrance window.

3.1.2 Vessel and thermistor probes

The core of the detector is a plane-parallel Pyrex vessel mounted inside the water tank, positioned with its face parallel to the entrance window and adjustable in depth relative to that window. The vessel is positioned on a dedicated holder, which itself is mounted on a horizontal positioning bar, ensuring accurate and reproducible placement during measurements. A schematic overview of the vessel is shown in figure 3.4. The vessel contains two lateral ports used to insert the thermistor probes and a third port for filling and bubbling (see section 3.2.2). Two similar vessels were used throughout this work, and more details about the exact dimensions are given in the following chapters.

A thermistor is a temperature-sensitive resistor that is used as a thermometer. Temperature is measured with thermistor beads encapsulated in conically shaped glass pipettes, referred to as the thermistor probes (figure 3.5). Inside the vessel, the two thermistor probes are positioned on opposite sides of the central axis, facing each other. The thermistors have a nominal resistance of $10\text{ k}\Omega$ at 4°C and a sensitivity of approximately $400\text{ }\Omega\text{ K}^{-1}$, enabling μK -level temperature resolution, which is necessary since the irradiation-induced temperature rise is only on the order of $240\text{ }\mu\text{K Gy}^{-1}$ [105].

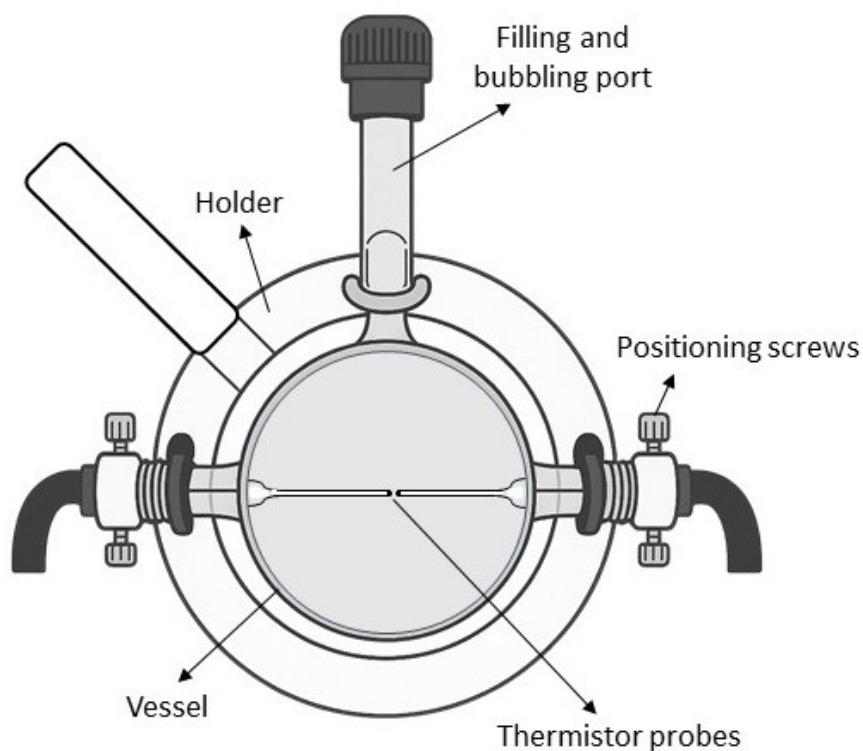


Figure 3.4: Schematic overview of the plane-parallel glass vessel and the positioning of the thermistor probes. The vessel contains two ports for inserting the thermistor probes and a third port for filling and bubbling of the vessel. Fine adjustment screws allow for precise positioning of the thermistor probes in the vessel. The vessel is mounted on a dedicated holder for placement inside the water calorimeter.

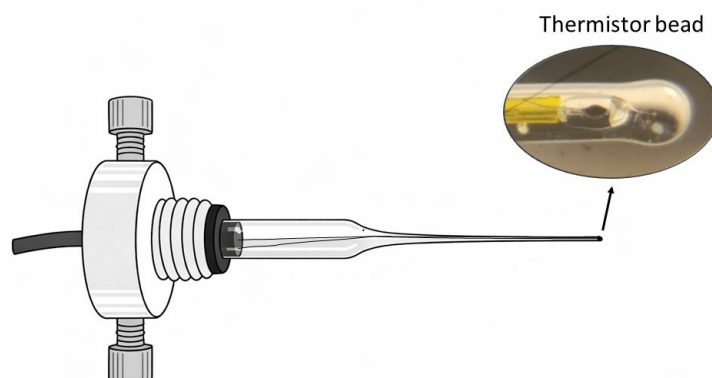


Figure 3.5: Schematic representation of a thermistor probe and picture of the probe tip containing the thermistor bead.

3.1.3 Electronics and bridge circuit

The small temperature rise measured by the thermistor probes is converted into an electrical signal using an AC-excited active bridge combined with a lock-in amplifier. All electronic components are shown in figure 3.1, while figure 3.6 presents a simplified schematic of the bridge circuit.

The thermistors inside the calorimeter vessel form one arm of an electrical bridge, while a high-precision resistor decade box (Hars-X series) forms the reference arm. The bridge is excited with a sinusoidal voltage provided by the lock-in amplifier (SR830 DSP, Stanford Research Systems). When the resistances of both arms are equal, the bridge is balanced and the voltage at the bridge output node (point A in figure 3.6) is zero. A change in thermistor resistance caused by a temperature rise during irradiation unbalances the bridge and produces a small sinusoidal voltage at this node. The measured quantity is therefore the voltage at point A, which is proportional to the thermistor resistance change and, through calibrations, to the temperature rise induced by the irradiation.

To achieve the sub-microkelvin temperature resolution required for water calorimetry, the bridge is implemented as an active AC bridge rather than a conventional passive Wheatstone bridge. Following the design of Seuntjens [107], two low-noise OP177 operational amplifiers generate two excitation voltages of equal amplitude and opposite phase. One drives the thermistor arm, while the other drives the arm containing the decade resistor. This active

configuration allows the bridge output to be measured relative to a stable ground reference instead of as a difference between two voltages, which reduces electronic noise and improves stability.

The lock-in amplifier both supplies the excitation signal and measures the voltage at point A. Using phase-sensitive detection at the excitation frequency, it extracts only the sinusoidal component generated by the bridge imbalance. In this way, resistance changes corresponding to temperature rises of only a few microkelvin can be resolved with high precision.

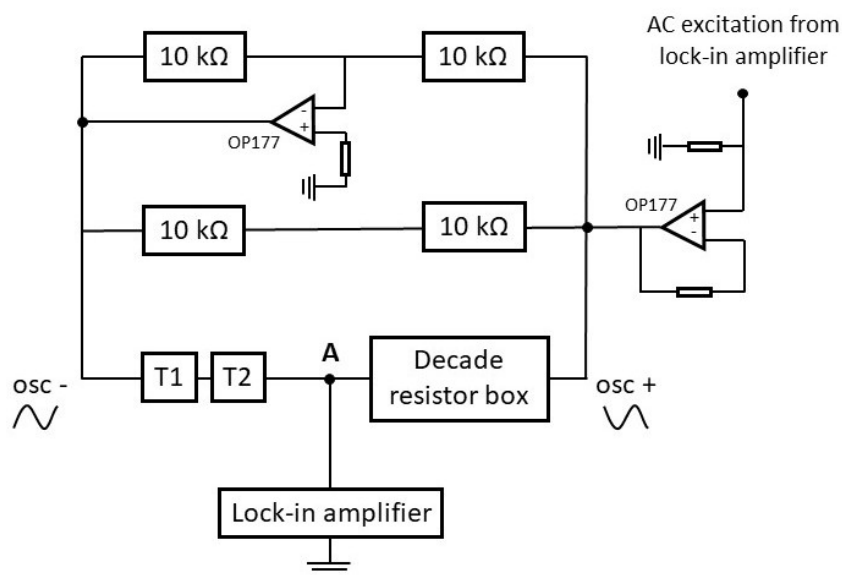


Figure 3.6: Simplified bridge schematic. T1 and T2 stand for thermistor 1 and 2. Figure is adjusted from [105].

A capacitor decade box (IET Labs, CS-301L) is used to balance the capacitive component of the signal. The operational amplifiers are powered by a low-noise power supply (Aim-TTi EL302R).

In addition to the thermistors inside the vessel, the three RTD probes monitor the bulk water temperature of the calorimeter. These RTDs are read out by a Keithley 2002 digital multimeter operating in four-wire resistance mode and are used to ensure that the calorimeter remains stable at $(4.0 \pm 0.1)^\circ\text{C}$ during operation.

All electronic signals from the lock-in amplifier and the multimeter are read out via GPIB and recorded using the H₂O-run acquisition software [105]. The resistor decade box, located in the control room, allows the bridge to be calibrated by introducing known resistance changes while keeping it isolated from the radiation area.

3.2 Operation of the water calorimeter

3.2.1 Calibrations

As stated before, a water calorimeter is considered as a primary standard technique because it determines absorbed dose to water without the need for cross-calibration to any radiation instrument. In principle, when temperature is defined, a calorimeter can measure dose. In this work, temperature is not measured directly, but it is obtained from a voltage measurement induced by a change in the thermistors' temperature-dependent resistance. To operate the calorimeter, three distinct calibration relationships are required and are presented in the following subsections.

RTD probes

The three RTD probes were calibrated against a digital reference thermometer (KM20REF, Comark) with an UKAS Calibration Certificate. For the calibrations, the probes were placed directly in the refrigerator's cooling-fluid bath. Each RTD probe was connected to the Keithley 2002 digital multimeter in 4-wire resistance mode to read their resistance. The temperature range covered was -4°C to 12°C by adjusting the refrigerator temperature in 1°C steps. At each increment, the bath was allowed to reach thermal equilibrium before measurements were taken. The reference thermometer provided the bath temperature, after which 15 resistance readings per RTD were recorded at that temperature. For each probe, these data yielded a calibration curve of resistance in function of temperature over the stated range.

Thermistor probes

The thermistor probe calibrations were also carried out in the refrigerator's cooling-fluid bath across -4°C to 12°C in 1°C intervals. At each interval and for each probe, 15 resistance readings were recorded, only after the resistance drift fell below 0.005%, indicating a very stable bath temperature.

The resistance R of the thermistors as function of temperature T is described

by the following relationship:

$$\ln R = a + \frac{b}{T} + \frac{c}{T^2}, \quad a, b, c \in \mathbb{R}. \quad (3.1)$$

A solution to the relation in Eq. (3.1) is:

$$R = R_0 \exp \left[\beta \left(\frac{1}{T} - \frac{1}{T_0} \right) \right], \quad (3.2)$$

where $T_0 = 25^\circ\text{C}$ (298.15 K), and R_0 and β are functions of temperature given by:

$$\beta(T) = b + \frac{2c}{T} \quad (3.3a)$$

$$R_0(T) = \exp \left[a + \frac{\beta(T)}{T_0} - \frac{c}{T^2} \right] \quad (3.3b)$$

A thermistor calibration curve is shown in figure 3.7. As all water calorimetry measurements are performed in a small temperature range around 4°C , the slowly varying functions $\beta(T)$ and $R_0(T)$ are approximated as constants for each thermistor. This approximation is obtained by evaluating $\beta(T)$ and $R_0(T)$ at 3.9°C , 4.0°C and 4.1°C and taking their average values.

The sensitivity of a thermistor is the relative resistance change per temperature change, and is defined as

$$S = \frac{1}{R} \frac{dR}{dT} = -\frac{\beta}{T^2}. \quad (3.4)$$

This sensitivity is used to convert measured resistance changes into temperature changes during the calorimetric measurements.

The uncertainty on the thermistor sensitivity was estimated by propagating the uncertainty on the absolute temperature of the reference thermometer ($\pm 0.065^\circ\text{C}$), through the relation described in equation 3.4. As $\beta(T)$ varies only weakly with temperature (approximately 0.006 % over 0.1°C around 4°C), its contribution is small compared to that arising from the explicit temperature dependence in the sensitivity expression. The resulting relative standard uncertainty on the thermistor sensitivity was estimated to be on the order of 0.07%.

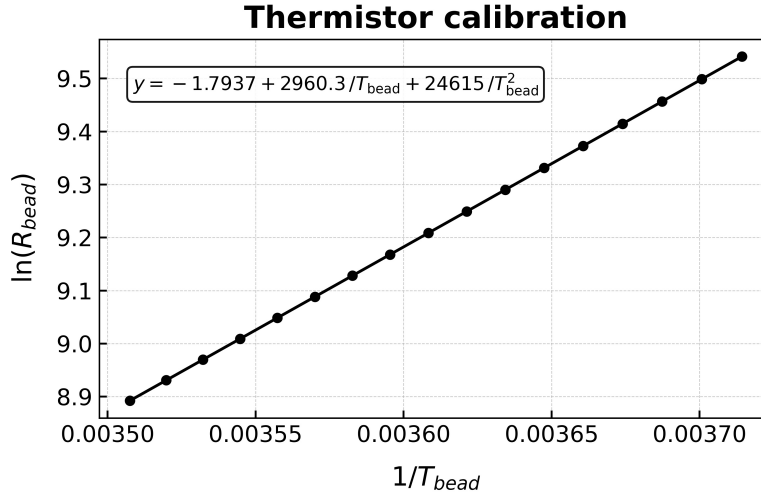


Figure 3.7: Thermistor calibration curve. The quadratic fit to the data points allows to determine $\beta(T)$ and $R_0(T)$ for each thermistor.

Bridge calibrations

The lock-in amplifier reports a non-zero voltage whenever the bridge is unbalanced, i.e. when the thermistor resistance differs from the decade-box resistance. An imbalance can arise from a temperature change during irradiation, which modifies the thermistors' resistance, or by deliberately adjusting the decade box. The latter is used to calibrate the bridge, linking a voltage change to a known resistance change. The calibration procedure starts with a balanced bridge, giving a (near) zero output of the lock-in amplifier. Then, the resistance of the decade box is changed by $1\ \Omega$, while recording the corresponding voltage change. A typical calibration curve is shown in figure 3.8.

The uncertainty on this calibration was estimated by combining a type A component, obtained from repeated calibration measurements, with a type B component arising from the accuracy of the applied resistance change. The latter is determined by the specified accuracy of the decade resistor box ($\pm 0.01\%$), corresponding to an uncertainty of $\pm 1 \times 10^{-4}\ \Omega$ for a $1\ \Omega$ step. The combined uncertainty on the calibration is, however, dominated by the type A component and is estimated to be on the order of 0.2% .

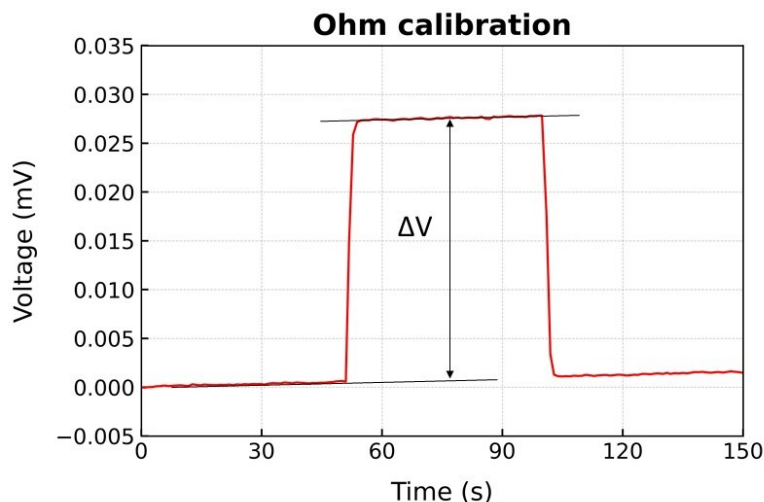


Figure 3.8: Ohm calibration curve.

3.2.2 Preparation of the vessel

Before each measurement campaign, the calorimeter vessel is prepared in a specific way to ensure successful measurements and avoid the so-called heat defect (see section 3.3.3). The vessel and thermistor probes are first thoroughly cleaned with deionized water, after which the thermistor probes are positioned inside the vessel. The probes are positioned as carefully as possible, and separated by approximately 2 mm on the central axis. Four plastic adjustment screws allow for precise positioning and a traveling microscope is used to verify the exact location of the probes inside the vessel. The vessel is then rinsed with deionized water followed by ultrapure water. The vessel is filled with ultrapure water provided by a Millipore water purification system (Synergy UV). Subsequently, the water in the vessel is bubbled with hydrogen (99.9999%, Alphagaz) for at least three hours through a polytetrafluorethylene (PTFE) tube inserted through the dedicated bubbling port. At the end of the the bubbling, the tube is removed and the vessel is sealed. The vessel is subsequently pre-irradiated with roughly 150 Gy to establish a steady-state heat defect. Finally, it is placed in the cooled calorimeter at the required measurement depth approximately 24 h before the first measurement to allow thermal stabilization.

3.2.3 Measurement procedure and signal analysis

The calorimeter is set up 24 h before the measurements to start the cooling of the water down to 4 °C. Approximately two hours before the actual measurements,

the magnetic stirrer is switched off to allow the water temperature to stabilize. A typical measurement run (figure 3.9) consists of three phases: a pre-drift period, the irradiation period, and a post-drift period. During the pre-drift period, the temperature signal is recorded before the start of the irradiation. This is followed by the irradiation period, during which the absorbed dose causes a temperature rise in the water. After the beam is switched off, the post-drift period is recorded. The voltage change caused by the irradiation is obtained by linearly extrapolating the pre- and post-drift curves to the mid-irradiation time and taking their difference. The calibrations described above are used to relate voltage to resistance (ohm calibrations) and resistance to temperature (thermistor calibrations). Using the definition of the thermistor's sensitivity (Eq. (3.4)), the temperature change can be determined as

$$\Delta T = \frac{\Delta R}{R} S^{-1} \quad (3.5)$$

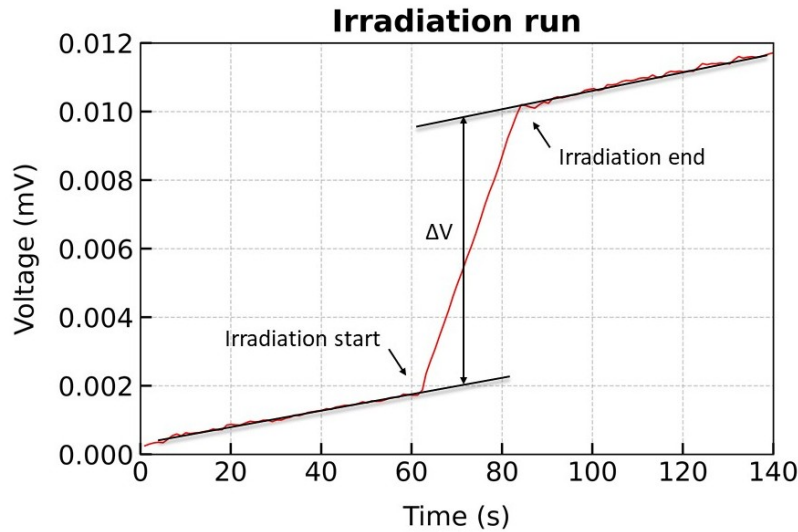


Figure 3.9: Typical irradiation run. Pre- and post-drift curves are measured for every irradiation. The voltage change (ΔV) caused by the irradiation is obtained by linearly extrapolating the pre- and post-drift curves to the mid-irradiation time.

Measurements are taken in blocks of approximately 10 consecutive runs, followed by a one-hour pause to re-stabilize the water temperature. During the first five minutes of each break, the magnetic stirrer is turned on to remove any

built-up thermal gradients. This cycle of acquisition blocks and stabilization pauses is repeated until the required statistics are achieved. Bridge calibrations are repeated throughout the session.

3.3 Correction factors

In principle, calorimetry is straightforward: the absorbed dose to water is obtained by multiplying the specific heat capacity of water by the measured temperature rise, as shown in equation 2.4. In practice, however, several correction factors must be applied to account for non-ideal conditions in the measurement process and to ensure an accurate determination of the absorbed dose. These corrections will also be discussed in the subsequent chapters of the individual measurement campaigns, but for completeness they are introduced here as well. The uncertainty associated with each correction factor is discussed in the experimental chapters where relevant.

Taking all relevant effects into account, the dose determination becomes:

$$D_w = c_w \Delta T k_c k_p k_{HD} k_{dd} k_\rho \quad (3.6)$$

where k_c corrects for the conductive heat transfer (3.3.1), k_p for the perturbation of the beam (3.3.2), k_{HD} for the heat defect mentioned above (3.3.3), k_{dd} for the non-uniformity of the lateral dose profile (3.3.4) and k_ρ for the difference in water density at 4 °C and room temperature (3.3.5).

3.3.1 Conductive heat transfer

Heat transfer occurs within the calorimeter during and after irradiation as a result of temperature gradients generated by non-uniformity of the dose deposition and the presence of non-water materials with different thermal properties. The water calorimeter is operated at 4 °C, the temperature around which water reaches its maximum density. Under these conditions, convective heat flow is minimal and can therefore be neglected [108, 109]. As a result, conductive heat transfer becomes the dominant mechanism influencing the calorimetric signal.

To account for this effect, a conductive heat transfer correction, k_c is applied. This correction factor is defined as the ratio of the ideal temperature rise that would be observed in the absence of conductive heat transfer to the actual temperature rise when conduction is present.

The correction is quantified by performing finite-element simulations using the COMSOL Multiphysics software (version 6.0, COMSOL AB). The finite element method (FEM) is a numerical technique for solving partial differential equations by discretizing the geometry into a finite number of small elements and approximating the solution within each element. This allows complex geometries and boundary conditions to be treated in a computationally efficient manner. In the absence of convection, the heat transfer equation is given by

$$\rho c_p \frac{\partial T}{\partial t} + \nabla \cdot (-k \nabla T) = Q \quad (3.7)$$

where ρ is the density, c_p the specific heat capacity at constant pressure, k the thermal conductivity, and Q the heat source [110]. The heat transfer equation is solved in both time and space using a simplified model of the calorimeter geometry. The simulations include the water tank, the calorimeter vessel, and a simplified representation of the thermistor probes. The full geometry is meshed, and the temporal evolution of the temperature field is calculated using the same timing as during the experiments, including the pre-drift, irradiation and post-drift phases. In addition, the same number of consecutive irradiations as during the measurements are simulated, allowing for residual thermal effects from previous irradiations to be taken into account. This temporal modeling is essential, as the thermal diffusivity of water is relatively low ($\alpha \approx 1.4 \times 10^{-7} \text{ m}^2 \text{ s}^{-1}$), resulting in heat redistribution occurring on time scales of several seconds over millimeter distances. As a result, the temperature field continues to evolve during and after irradiation.

Accurate modeling of conductive heat transfer requires detailed knowledge of the calorimeter geometry, material properties, initial temperature distributions, and the temporal structure of the irradiation. Different irradiation conditions, such as scattered versus scanned fields and different accelerator types, require distinct approaches to model the spatial and temporal characteristics of the beam. The specific modeling strategies adopted for each measurement campaign are described in detail in the subsequent chapters.

3.3.2 Beam perturbation

The presence of non-water materials within the calorimeter, in particular the glass vessel and the thermistor probes, perturbs the radiation field at the measurement location and can therefore influence the measured dose. A beam perturbation correction factor, k_p is introduced to take this into account. The perturbation correction factor is determined in this work using Monte Carlo

simulations performed using GATE/Geant4. The Monte Carlo method is a stochastic technique that simulates the transport and interactions of individual particles in matter by sampling from probability distributions describing physical processes such as scattering and energy deposition.

The correction is defined as the ratio of the absorbed dose obtained from two simulations: one employing an idealized geometry in which all materials are replaced by water, and one using a realistic model of the calorimeter geometry that includes the glass vessel and thermistor probes with their correct material compositions and densities. In both cases, the absorbed dose is scored in a small volume surrounding the thermistor position. The resulting ratio provides a direct estimate of the beam perturbation introduced by the calorimeter components. The simulated beams are modeled to reproduce the experimental beam characteristics as closely as possible. For scanned beams, the temporal delivery structure is not explicitly modeled, and the beam is assumed to be delivered instantaneously.

3.3.3 The heat defect

Early implementations of water calorimetry showed systematic discrepancies when compared with graphite calorimeters and ionization chamber measurements, with differences on the order of several percent [111–113]. Such deviations were far too large to be explained by the stated measurement uncertainties and prompted further investigation into the behavior of water under irradiation. Subsequent studies revealed that, although the water volume was thermally isolated, dissolved gases and impurities could participate in radiation-induced chemical reactions and altered the amount of heat released [114]. This effect is described as the heat defect, defined as the difference between the energy absorbed from the radiation field and the portion of that energy that appears as heat.

When radiation passes through water, clusters of ionized and excited species are formed along the particle track. Within these clusters, highly reactive species are produced, which may undergo recombination reactions that form stable products. Some of these species escape from the cluster into the bulk liquid, where they can participate in further chemical reactions. The balance between recombination within the clusters and reactions in the bulk determines the chemical energy released or stored, and thus the heat defect. Impurities present in the water can act as scavengers for the species that escape the spurs, thereby perturbing this balance [66].

The yields of the different species that escape the cluster are described by the G-values, defined as the number of species formed per 100 eV of deposited energy. These G-values depend on the linear energy transfer of the radiation. As LET increases, the density of the ionization events along the particle track increases, leading to overlap of clusters and reactions within the clusters becoming more important. As a result, fewer highly reactive species escape into the bulk liquid. The chemical reactions rates themselves are independent of LET, and therefore any dependence of the heat defect on LET arises through the G-values [66].

Modern water calorimeters mitigate these effects by enclosing the thermistor probes within a glass vessel. This design allows the chemical composition of the water surrounding the probes to be tightly controlled, unlike the larger open water volume of the calorimeter. Both experimental and theoretical work has been performed to investigate the heat defect in water calorimetry under different chemical conditions [67, 115–117]. These studies examined ultrapure water saturated with various gases, including nitrogen, hydrogen and mixtures of oxygen and hydrogen. From these investigations, ultrapure water saturated with hydrogen was identified as the optimal system for eliminating the heat defect. In practice, however, trace concentrations of dissolved oxygen are always present and give rise to an initial exothermic response during irradiation. This effect corresponds to the depletion of oxygen and can be removed by sufficient pre-irradiation of the system. Once the residual oxygen has been consumed, a chemical steady state is reached and the net heat defect becomes zero [118].

3.3.4 Non-uniformity of the dose profile

The correction factor k_{dd} accounts for the difference between the dose measured at the thermistor probes location and the dose at the central axis of the beam. Because each thermistor is positioned approximately one millimeter off-axis, the measured temperature rise corresponds to the local dose at the probe locations rather than the central-axis dose. To compensate for this, the average dose measured by the thermistors is scaled using the lateral dose profiles. In most external radiation therapy fields, the dose distribution around the central axis is highly uniform, resulting in a very flat lateral profile. As a consequence, the magnitude of this correction is typically small, especially given that the thermistor probes are displaced by only about 1 mm from the central axis.

3.3.5 Water density

The correction factor k_ρ accounts for the difference in water density between the calorimeter operating temperature (4 °C) and the water temperature at

which ionization chambers are calibrated (room temperature). As the density of water varies slightly with temperature, the effective measurement depth will vary slightly between the calorimeter and ionization chamber measurements. This depth shifts translates into a small change in the local absorbed dose, which is corrected using the depth-dose curves. For particle beams, measurements in this work are performed in the plateau region of the depth-dose distribution, where dose gradients are minimal. As a result, the corresponding correction is generally close to unity.

Summary and outlook

The experimental studies presented in the following chapters build directly upon the calorimetric framework described here. For each measurement campaign, the operational procedures, calibration methods, and correction strategies are applied and adapted to the specific beam conditions under investigation. The subsequent chapters focus on the experimental determination of beam quality correction factors in photon and particle beams, with the water calorimeter serving as the reference for absorbed dose to water.

Chapter 4

Evaluation of ionization chambers for photon reference dosimetry

The content presented in this chapter corresponds to the published article: *Assessment of compact cylindrical and plane-parallel ionization chambers as reference dosimeters in high-energy photon beams*. [Physica Medica 145 \(2026\) 105799](#).

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4.1 Summary

Objective: To assess the performance of compact cylindrical and plane-parallel ionization chambers that are currently not included in international dosimetry protocols in high-energy photon beams, and evaluate their suitability as reference chambers.

Approach: Four types of cylindrical (IBA RAZOR™ Nano, CC01, CC04, CC08) and two types of plane-parallel (IBA PPC40, PPC05) chambers were investigated. Measurements were performed for five different photon beams, with TPR_{20,10} values ranging from 0.680 to 0.764. Polarity, recombination and beam quality correction factors (k_Q) were determined for all chamber types across all beam qualities. The k_Q -factors were obtained by direct calibration against a water calorimeter. Chamber stability was evaluated based on available long-term calibration coefficients.

Main results: The experimentally determined k_Q -factors exhibited a standard uncertainty ($k = 1$) between 1.1% and 1.5%, with the largest sources of uncertainty stemming from the heat transfer within the calorimeter vessel and the chamber calibration coefficients. Results were consistent within 0.2% for chambers of the same type. Comparison with literature data from experiments and Monte Carlo simulations demonstrated strong agreement for all chambers except the CC01, where discrepancies are likely due to the presence of a steel electrode. Polarity and recombination correction factors were small and stable across all investigated beam qualities. Cylindrical chambers showed good stability, with somewhat larger variations observed for plane-parallel chambers.

Significance: This work expands the database of available k_Q -factors for ionization chambers not currently included in dosimetry protocols and provides experimental data on their behavior in high-energy photon beams, contributing to their evaluation for use in reference dosimetry.

4.2 Introduction

Based on international codes of practice such as IAEA TRS-398 Rev. 1 [6] or AAPM's TG-51 [70] and its Addendum [119], ionization chambers are recommended to determine absorbed dose to water in high-energy photon beams. Ideally, these ionization chambers are calibrated in a reference beam with the same beam quality Q as the user beam, and dose to water $D_{w,Q}^{ion}$ is obtained by multiplying the corrected chamber output M_Q with the calibration coefficient $N_{D,w,Q}$ obtained in this beam quality according to the following formula:

$$D_{w,Q}^{ion} = M_Q N_{D,w,Q} \quad (4.1)$$

In practice, the user beam (Q) differs from the reference beam (Q_0), and a correction needs to be applied to take this difference in beam qualities into account. Applying this beam quality correction factor k_{Q,Q_0} gives:

$$D_{w,Q}^{ion} = M_Q N_{D,w,Q_0} k_{Q,Q_0} \quad (4.2)$$

When the reference beam is a ^{60}Co beam, which is commonly the case, Q_0 is omitted, and the correction factor is simply referred to as k_Q . As this convention is used throughout this work, we will consistently refer to the beam quality correction factor as k_Q .

Current international dosimetry protocols recommend a limited set of ionization chambers as reference instruments, typically cylindrical chambers with cavity volumes between 0.1 and 1 cm³, ensuring sufficient sensitivity in high-energy photon beams [82, 120]. Plane-parallel chambers are currently excluded as reference chambers due to some studies reporting larger variations of ion recombination and polarity corrections, chamber leakage and k_Q values within the same chamber type [121–125]. Despite this, other studies have explored the feasibility of using these ionization chambers for reference dosimetry in high-energy photon beams, highlighting the need for further experimental investigation [81, 82, 126, 127]. The most recent Codes of Practice (CoP) also define criteria for assessing the suitability of ionization chambers as reference dosimeters, including chamber stability (changes in calibration coefficient < 0.3%) and small and reproducible polarity (< 0.4%) and ion recombination effects [6, 119, 128, 129].

In this context, the objective of this work is to assess the suitability of cer-

tain compact cylindrical (IBA RAZOR™ Nano, CC01, CC04 and CC08) and plane-parallel (IBA PPC05 and PPC40) ionization chambers as potential reference chambers in high-energy photon beams. This is achieved through the experimental determination of k_Q -factors using water calorimetry, along with measurements of polarity and recombination correction factors, which are critical for evaluating chamber performance. Where available, historical calibration data were also evaluated to assess chamber stability. By evaluating these parameters across different beam qualities and comparing to available existing data, this study aims to provide evidence on whether these chambers meet the criteria for reference dosimetry, and to expand the current database of available k_Q -factors for chambers not included in international dosimetry protocols.

4.3 Materials and methods

4.3.1 Irradiation conditions

All the measurements presented were performed at IBA Dosimetry (Schwarzenbruck, Germany) using an Elekta Synergy linear accelerator. Following TRS-398 Rev. 1, the k_Q values are provided as a function of the beam quality index $\text{TPR}_{20,10}$. The study involved five different photon beams: 6 MV FFF (flattening filter free), 6 MV, 10 MV FFF, 10 MV and 15 MV with corresponding beam qualities $\text{TPR}_{20,10}$ of 0.680, 0.691, 0.715, 0.745, and 0.764, respectively. Measurements were conducted at a water-equivalent measurement depth of 10 cm, as recommended by the IAEA TRS-398 Rev. 1 protocol [6]. To confirm the stability of the beam during the entire calorimetry campaign, a cylindrical chamber CC13 was used in the corner of the field as a monitor chamber. To be sure that the monitor chamber doesn't influence the results, a field size of 20 cm $\times$ 20 cm was used instead of the recommended 10 cm $\times$ 10 cm.

4.3.2 Setup and operation of the water calorimeter

The water calorimeter used in this study consists of a 30 cm $\times$ 30 cm $\times$ 30 cm water tank made out of PMMA, which is surrounded by two layers of 5 cm thick polystyrene for thermal insulation. During the calorimetric measurements, the calorimeter is operated at 4 °C to avoid convective heat transfer in the water [130]. The calorimeter is designed for horizontal beams and has a 10 cm $\times$ 10 cm entrance window with a thickness of 1 mm made out of PMMA.

The core of the calorimeter is a plane-parallel glass vessel (diameter 7.9 cm, height 2.36 cm, entrance/exit windows 1.12 mm), designed at the National Research Council Canada (NRC), which is positioned inside the water tank.

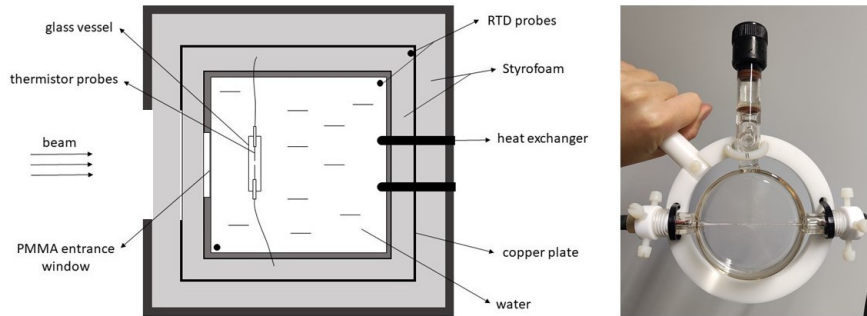


Figure 4.1: Left: Schematic of the water calorimeter and its main parts. Right: plane-parallel glass vessel with the two thermistor probes inside.

Inside the vessel, two thermistor beads measure the actual temperature rise caused by the irradiation. These thermistor beads are encapsulated in conically-shaped glass probes and have a radius of 0.25 mm. The probes are positioned on opposite sides with their respective sensitive head located at 1 mm of the central axis of the vessel and 3.4 mm below the entrance window. The positioning of the thermistors inside the vessel is done using a traveling microscope. The vessel is positioned in such a way that the thermistor probes are at the desired water-equivalent measurement depth of 10 cm.

Ideally, the thermistor probes would be placed further away from the entrance window to reduce the heat transfer from the surrounding environment. However, this specific vessel was originally designed for use in low-energy electron beams, where space constraints limited the possible geometry. While this design is not optimal for use in photon beams and may introduce larger correction factors and associated uncertainties, it is suitable for assessing the consistency of k_Q values.

Figure 4.1 shows a schematic of the water calorimeter and its most important parts and the glass vessel with the two thermistor probes positioned inside.

The two thermistor probes are integrated in an electronic circuit to convert the output signal to temperature. A typical irradiation run is given in figure 4.2. Before and after each irradiation, 60 s of pre- and post-drift are measured. To get the temperature rise due to the irradiation, the pre- and post-drift curves are linearly extrapolated to mid-irradiation time. For the post-drift curve, the first 10 seconds after the end of the irradiation are excluded due to the thermistor material causing an over-response of the signal.

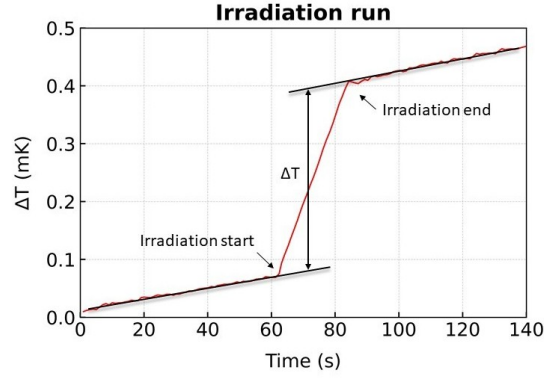


Figure 4.2: A typical irradiation run, with 60 s of pre-drift and 60 s of post-drift. To get the signal due to the irradiation, the pre- and post-drift curves are linearly extrapolated to the mid-irradiation time.

4.3.3 Calorimetric determination of D_w

The calorimetric determination of absorbed dose to water is done using the following formula:

$$D_{w,Q}^{cal} = c_w \Delta T k \quad (4.3)$$

where c_w is the specific heat capacity of water at 4 °C (which was taken to be $4204.8 \text{ J kg}^{-1} \text{ K}^{-1}$ [131]), ΔT the temperature rise due to the irradiation and k the product of several correction factors.

Correction factors

The following correction factors are applied to the response of the calorimeter to account for any non-ideal conditions:

$$k = k_c k_p k_{dd} k_\rho k_{HD} \quad (4.4)$$

The factor k_c corrects for the conductive heat transfer in the calorimeter considering geometric and material properties, as well as variations in the local dose profile during and after the irradiation. The correction factor is defined as the ratio of the ideal temperature rise, i.e. without conduction, and the actual temperature rise, i.e. with conduction. The heat transport within the

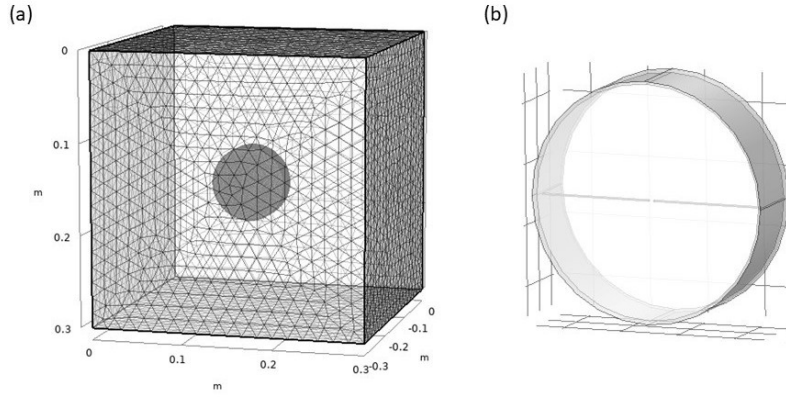


Figure 4.3: Model of the water calorimeter in COMSOL Multiphysics. (a) Full model with used mesh and (b) close-up of the vessel and thermistor probes.

calorimeter is simulated by performing finite-element simulations using the software COMSOL Multiphysics (version 6.0). A 3D geometry of the water tank, including the vessel and simplified model of the thermistors, has been implemented (see figure 4.3). The 3D dose distribution inside the water tank, based on the percent depth dose (PDD) profiles and lateral dose profiles, was used as a heat source to solve the heat transfer equation in both time and space. The doses in the non-water materials were converted using Monte Carlo simulations. k_c -values were simulated following the temporal structure used during the measurements (i.e. same number of consecutive irradiations, same time between two runs, same pre- and post-drift intervals, etc).

The factor k_p corrects for the perturbation of the beam caused by the presence of non-water materials in the beam path. It is defined as the ratio of the dose to water at the thermistor position ignoring all non-water materials to the dose to water in the actual situation (i.e. with non-water materials). This correction is obtained through Monte Carlo simulations, using GATE/Geant4 (v9.0, physics list `emstandard_opt3`). Two separate simulations are conducted using a full 3D model of the calorimeter with simplified model of the thermistors: one simulation considers every material as water, and the other involves the real material properties.

The factor k_{dd} corrects for the non-uniformity of the lateral dose profile, as the thermistors are not located at the central axis of the beam but 1 mm away. This correction is based on the lateral dose profiles of the various beams. Given the proximity of the thermistors to the central axis and the relatively flat dose

profiles around this axis, the correction factor is taken to be unity, with an associated uncertainty of 0.1%.

The factor k_ρ corrects for the difference in water density at different temperatures. As calorimetric measurements are performed at 4 °C and the ionometric measurements at room temperature (20 °C in this case), there will be a discrepancy in water density, resulting in a slight difference in measurement depth. By knowing the water density at these temperatures and the depth dose profile of the beam, we can apply the necessary correction. As the density of water is 0.18% higher at room temperature than at 4 °C, the difference in measurement depth at 10 cm will be 0.18 mm. Based on the depth dose profiles, this results in correction factors ranging from 1.0007 to 1.0009 for all conditions.

The factor k_{HD} corrects for the heat defect, which is defined as the difference between the energy absorbed from the radiation and the energy appearing in the form of heat. This effect is caused by the radiolysis of water and endo- and exothermic chemical reactions due to impurities in the water. Previously, calculations based on the radiolysis of water have been done for various aqueous systems by Klassen and Ross [116]. Based on this work, it was found that hydrogen-saturated ultrapure water reaches a steady state after pre-irradiation and therefore a zero net heat defect. In this case, the correction factor is assumed to be unity with an uncertainty of 0.14% [132]. In this work, the vessel is filled with ultrapure water (Synergy UV system, ppb < 5) to minimize the amount of impurities inside. Afterwards, the water is saturated with hydrogen (Alphagaz, purity 99.9999%) through bubbling for at least 3 hours. Before the actual measurements, the vessel is pre-irradiated with a dose of approximately 150 Gy to make sure the steady state heat defect is reached [118].

4.3.4 Ionometry

Four types of IBA Dosimetry cylindrical ionization chambers have been used: RAZOR™ Nano (#21216, #21218), CC01 (#8805, #11122), CC04 (#8835, #8836) and CC08 (#7858), with cavity volumes of 0.003, 0.01, 0.04 and 0.08 cm³, respectively. The measurements were done with two chambers of the same type, except for the CC08, of which only one chamber was used. Two types of IBA Dosimetry plane-parallel chambers have been used: three PPC40 (#162, #508, #512) (electrode spacing 2 mm and collecting electrode diameter 16 mm) and one PPC05 (#194) (electrode spacing 0.6 mm and collecting electrode diameter 10 mm). The chambers were set in the water calorimeter using dedicated holders. All experimental conditions were the same as the ones used for the calorimetric measurements, except the water in the calorimeter was at

room temperature. The cylindrical chambers were positioned with their central electrode at 10 cm, while for the plane-parallel chambers the inner surface of the entrance window was positioned at 10 cm as recommended by TRS-398 Rev. 1. The N_{D,w,Q_0} -value of all chambers was determined at the Secondary Standard Dosimetry Laboratory (SSDL) at IBA Dosimetry in a Cobalt-60 beam at the operating voltage. The calibrations done at the SSDL are in accordance with the IAEA TRS-398 Rev. 1 Code of Practice and traceable to the Primary Standard Dosimetry Laboratory of PTB-Braunschweig (Germany). For chambers for which previous calibration data were available, annual calibration coefficients measured at IBA Dosimetry over the period 2018–2025 were evaluated to assess chamber stability. All cylindrical chambers were used at the recommended operating voltage of +300 V while the plane-parallel chambers were used at –300 V.

All ionization chamber readings are corrected for temperature and pressure (k_{tp}), polarity (k_{pol}) and recombination (k_s) effects. To correct for the recombination effect, the two-voltage method was used with the second voltage being +100 V and –100 V for the cylindrical and plane-parallel chambers, respectively. Polarity and recombination corrections were measured for one chamber of each type and assumed to be the same for all chambers of the same type. The measurements performed in the FFF fields were also corrected for the volume averaging effect (k_{vol}) as described in TRS-483 [128, 129].

4.3.5 Determination of k_Q

Using the water calorimeter and the ionization chambers in the same conditions allows to directly compare the response of both devices in terms of absorbed dose to water:

$$D_{w,Q}^{cal} = D_{w,Q}^{ion} = M_Q N_{D,w,Q_0} k_Q \quad (4.5)$$

Therefore, the beam quality correction factor, k_Q , can be derived as:

$$k_Q = \frac{D_{w,Q}^{cal}}{M_Q N_{D,w,Q_0}} \quad (4.6)$$

4.4 Results

4.4.1 Calorimetric determination of D_w

A total of 27 to 30 calorimeter runs were performed for each photon energy. The applied correction factors are presented in table 4.1 and the total uncertainty budget for the calorimetric determination of absorbed dose to water is provided in table 4.2. All quoted uncertainties are standard uncertainties (one standard deviation). Besides the uncertainty on the calorimeter output, which is type A, all other uncertainties are type B. The reproducibility of the calorimetric measurements, expressed as the standard error of the mean, ranged between 0.14% and 0.2% for all five beam qualities. The uncertainty on the specific heat capacity of water was taken to be 0.05% based on the work of Medin [95]. Uncertainties on the thermistor and electronic calibrations were also considered. Additionally, a positioning uncertainty of the measurement position in depth was considered, amounting to 0.3%. The positioning uncertainty of the thermistors within the calorimeter vessel was incorporated in the uncertainty of the individual correction factors.

$\text{TPR}_{20,10}$	k_c	k_p	k_{dd}	k_ρ	k_{HD}
0.680	0.899	0.997	1.000	1.001	1.000
0.691	0.897	0.996	1.000	1.001	1.000
0.715	0.899	0.989	1.000	1.001	1.000
0.745	0.898	0.989	1.000	1.001	1.000
0.764	0.899	0.988	1.000	1.001	1.000

Table 4.1: Correction factors applied to the calorimetric measurements per beam quality $\text{TPR}_{20,10}$. k_c corrects for conductive heat transfer, k_p for beam perturbation, k_{dd} for lateral beam non-uniformity, k_ρ for water density differences, and k_{HD} for the chemical heat defect.

The uncertainties associated with the different correction factors were evaluated for all five photon beams, revealing no significant variations between them. Overall, the total uncertainty on the calorimetric determination of absorbed dose to water is estimated to be 0.93%.

While most correction factors are relatively small, the finite-element simulations indicated that heat transfer inside the calorimeter vessel (k_c) requires a substantial correction factor of approximately 10%. This large value is attributed to the proximity of the thermistors to the glass vessel, which substantially influences the conductive heat transfer nearby the thermistor probes. Additional

Quantity	Relative standard uncertainty (%)
Calorimeter output	0.14-0.2
Specific heat capacity c_w [95]	0.05
Electronic calibration	0.2
Thermistor calibration	0.07
Positioning	0.3
Heat transfer correction k_c	0.8
Beam perturbation correction k_p	0.1
Heat defect k_{HD} [132]	0.14
Density correction k_ρ	< 0.01
Dose-profile non-uniformity k_{dd}	0.1
$D_{w,Q}^{cal}$	0.93

Table 4.2: Uncertainty budget for the calorimetric determination of absorbed dose to water ($k = 1$).

simulations using COMSOL were performed to investigate this correction for different distances between the thermistors and the glass vessel. These simulations confirmed that the closer the thermistors are to the entrance window, the larger the conductive heat transfer correction required, as shown in figure 4.4. Ideally, to minimize the conductive heat transfer, the thermistor probes should be between 10 mm and 12 mm from the entrance window. However, due to the design of the glass vessel, it was not possible to position the thermistor probes further away from the entrance window than 3.4 mm. An uncertainty of 0.8% was estimated for this correction factor, accounting for the variations between the 10 consecutive irradiations and uncertainties in the modeling. Uncertainty assessment was carried out by performing parameter sweeps, systematically varying mesh resolution, material properties, geometric dimensions, solver tolerances and the input dose distribution.

In the work of Verpoest *et al.* [133], similar water calorimetry measurements were performed using the present vessel and a second vessel designed to yield smaller heat-transfer corrections (< 1%) in proton beams. The k_Q -factors obtained with the two vessels under identical irradiation conditions agreed within 0.2%, thereby increasing confidence in the heat transfer simulations applied in this work and in the resulting k_Q -factors, despite the large heat-transfer corrections required for the present work.

Based on the Monte Carlo simulations, the correction for perturbation of

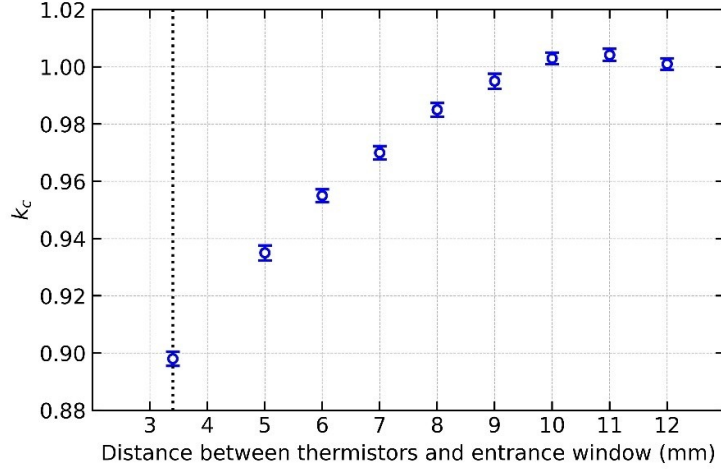


Figure 4.4: Conductive heat transfer correction k_c vs. the distance between the thermistors and the entrance window. The dotted vertical line represents the conditions used in this work. The uncertainty bars indicate the statistical uncertainty on the variation between 10 consecutive irradiation runs in the same conditions as during the measurements.

the beam is between 0.988 and 0.997 for all conditions. The uncertainty on this correction factor k_p includes the statistical uncertainty of the Monte Carlo simulations as well as type B uncertainties such as the physics model, material parameters and thermistor location.

As mentioned in section 4.3.3, the uncertainty on the heat defect is taken to be 0.14% based on the work of Krauss [132]. The uncertainty for the density correction was based on the uncertainty of the density of water and is smaller than 0.01% [134]. The uncertainty on the dose-profile non-uniformity is based on the measured dose profiles and estimated to be in the order of 0.1%.

4.4.2 Ionometric determination of D_w

In total, 7 cylindrical and 4 plane-parallel chambers were irradiated, and for each chamber, 10 readings were taken per condition. Corrections for temperature and pressure, polarity and recombination were applied for all conditions. Polarity and recombination correction factors for the cylindrical chambers are given in table 4.3 and for the plane-parallel chambers in table 4.4. These values were consistent across all five photon beams. As stated in IAEA TRS-398 Rev. 1, reference-class ionization chambers are expected to exhibit a polarity

effect below 0.4%. For the smallest volume chambers, this correction may slightly exceed that threshold. However, the polarity corrections generally remain small ($< 0.6\%$). The volume averaging correction was performed for the measurements in the FFF fields. For the cylindrical chambers, the volume averaging correction factor is assumed to be unity due to the small cavity length [128]. For the PPC05 and PPC40, the values are 1.001 and 1.0016 and 1.0016 and 1.003, for the 6 MV FFF and 10 MV FFF fields, respectively.

Beam	RAZOR TM Nano		CC01		CC04		CC08	
	k_s	k_{pol}	k_s	k_{pol}	k_s	k_{pol}	k_s	k_{pol}
6 MV FFF	1.007	0.999	1.004	1.006	1.003	1.004	1.007	1.000
6 MV	1.008	1.000	1.003	1.006	1.002	1.004	1.004	1.002
10 MV FFF	1.007	0.994	1.004	1.006	1.003	1.003	1.008	1.001
10 MV	1.007	0.995	1.006	1.003	1.002	1.003	1.005	1.001
15 MV	1.007	0.994	1.003	1.005	1.002	1.003	1.006	1.001

Table 4.3: Recombination and polarity correction factors for the cylindrical ionization chambers.

Beam	PPC05		PPC40	
	k_s	k_{pol}	k_s	k_{pol}
6 MV FFF	1.005	0.996	1.002	0.999
6 MV	1.005	0.995	1.003	0.999
10 MV FFF	1.004	0.997	1.004	0.999
10 MV	1.005	0.996	1.002	0.999
15 MV	1.005	0.996	1.003	1.000

Table 4.4: Recombination and polarity correction factors for the plane-parallel ionization chambers.

The total uncertainty budget for the different ionization chamber measurements is presented in table 4.5. The total uncertainty includes the uncertainty on the calibration coefficient, the correction factors, positioning and the statistical uncertainty of the chamber reading. The uncertainty on the chamber reading is type A, all other uncertainties are type B. A total uncertainty of 1.22% was obtained for the RAZORTM Nano chamber, with the biggest contribution being the uncertainty on the calibration coefficient N_{D,w,Q_0} of the chambers which was approximately 1.1%. The uncertainty on the calibration coefficient

of almost all other chambers is in the order of 0.37%, giving a total uncertainty of approximately 0.57% for those chambers. Only for the PPC40 #508 and PPC40 #512, the calibration coefficient had an uncertainty of 0.5%, which led to a total uncertainty of 0.66% on the measured absorbed dose to water with these chambers.

Quantity	Relative standard uncertainty (%)					
	RAZOR [™] Nano	CC01	CC04	CC08	PPC05	PPC40
Chamber reading	0.25	0.14	0.10	0.07	0.08	0.08
k_{tp}	0.20	0.20	0.20	0.20	0.20	0.20
k_s	0.11	0.11	0.11	0.11	0.10	0.10
k_{pol}	0.16	0.08	0.06	0.05	0.06	0.04
k_{vol}	0.20	0.20	0.20	0.20	0.20	0.20
Positioning	0.30	0.30	0.30	0.30	0.30	0.30
N_{D,w,Q_0}	1.10	0.37	0.37	0.37	0.37	0.50
Combined uncertainty	1.22	0.58	0.57	0.57	0.57	0.66

Table 4.5: Full uncertainty budget for the ionometric determination of absorbed dose to water ($k = 1$).

4.4.3 k_Q -factors

Using equation 4.6, we derived the final k_Q values for the six types of chambers across the five different beam qualities used in this study. The obtained values for all ionization chambers are summarized in table 4.6. For the RAZOR[™] Nano, CC01 and CC04 chambers, two chambers of each type were used, and the average k_Q value from these measurements is also given in table 4.6. In order to determine the combined standard uncertainty on the final beam quality correction factors k_Q , the standard uncertainty on the determination of absorbed dose to water of one chamber was combined with the standard deviation of the k_Q -factors of the same chamber type. For the CC08 and PPC05 chambers, only one of each type was measured. For the PPC40, the results of the three different chambers as well as the average of the three chambers are presented in table 4.6.

IC \ TPR _{20,10}	0.680	0.691	0.715	0.745	0.764
RAZOR™ Nano					
#21216	0.9910 ± 0.0152	0.9799 ± 0.0150	0.9828 ± 0.0150	0.9702 ± 0.0148	0.9709 ± 0.0149
#21218	0.9902 ± 0.0152	0.9789 ± 0.0150	0.9826 ± 0.0150	0.9679 ± 0.0148	0.9688 ± 0.0149
Average	0.9906 ± 0.0152	0.9799 ± 0.0150	0.9827 ± 0.0151	0.9691 ± 0.0149	0.9699 ± 0.0149
CC01					
#8805	0.9799 ± 0.0108	0.9794 ± 0.0108	0.9714 ± 0.0107	0.9693 ± 0.0107	0.9715 ± 0.0107
#11122	0.9786 ± 0.0108	0.9772 ± 0.0107	0.9729 ± 0.0107	0.9693 ± 0.0107	0.9711 ± 0.0107
Average	0.9793 ± 0.0108	0.9783 ± 0.0108	0.9722 ± 0.0107	0.9693 ± 0.0107	0.9713 ± 0.0107
CC04					
#8835	0.9942 ± 0.0108	0.9916 ± 0.0108	0.9808 ± 0.0107	0.9765 ± 0.0106	0.9752 ± 0.0106
#8836	0.9935 ± 0.0108	0.9913 ± 0.0108	0.9805 ± 0.0107	0.9777 ± 0.0107	0.9754 ± 0.0106
Average	0.9938 ± 0.0108	0.9915 ± 0.0108	0.9807 ± 0.0107	0.9771 ± 0.0106	0.9753 ± 0.0106
CC08					
#7858	0.9937 ± 0.0108	0.9902 ± 0.0108	0.9868 ± 0.0108	0.9752 ± 0.0106	0.9740 ± 0.0106
PPC05					
#194	0.9751 ± 0.0107	0.9764 ± 0.0107	0.9655 ± 0.0106	0.9600 ± 0.0105	0.9577 ± 0.0105
PPC40					
#162	0.9863 ± 0.0108	0.9847 ± 0.0107	0.9744 ± 0.0106	0.9693 ± 0.0106	0.9661 ± 0.0105
#508	0.9871 ± 0.0113	0.9842 ± 0.0112	0.9764 ± 0.0111	0.9692 ± 0.0111	0.9660 ± 0.0110
#512	0.9873 ± 0.0113	0.9844 ± 0.0112	0.9757 ± 0.0111	0.9673 ± 0.0110	0.9640 ± 0.0110
Average	0.9869 ± 0.0113	0.9845 ± 0.0113	0.9755 ± 0.0112	0.9686 ± 0.0111	0.9654 ± 0.0111

Table 4.6: Obtained k_Q -factors for the different ionization chamber types per beam quality TPR_{20,10} with their associated $k = 1$ uncertainty.

4.4.4 Chamber stability

For several ionization chambers (CC01 #8805, CC01 #11122, CC04 #8835, CC04 #8836, CC08 #7858, PPC05 #194 and PPC40 #162), annual calibration coefficients obtained at IBA Dosimetry between 2018 and 2025 were available and analyzed to assess chamber stability. For the RAZOR™ Nano chambers, no data was available. For the CC01 chambers, the total change in calibration coefficient over the seven-year period was approximately 0.2%. Year-to-year variations were generally below the 0.3% criterion recommended in TRS-398 Rev. 1, with the exception of one instance where a maximum deviation of 0.36% was observed. The observed variations were random in time, with no indication of a systematic drift. Similar behavior was observed for the two CC04 chambers and the CC08 chamber. In all cases, year-to-year variations remained below 0.3%, and the overall change in calibration coefficient over the full period was also below 0.3%. No temporal trend or long-term drift was identified. The plane-parallel chambers exhibited slightly larger variations. While year-to-year variations were generally small, isolated deviations of up to approximately 1.3% were observed for both chamber types. Nevertheless, the overall change in calibration coefficient over the whole period was approximately 0.5% for the PPC40 chamber and 0.6% for the PPC05 chamber. Despite these larger short-term variations, no systematic long-term drift was observed.

4.5 Discussion

4.5.1 Cylindrical ionization chambers

For most of the chambers used in this work, k_Q -factors for some beam qualities have previously been determined through either experimental methods or simulations. However, no experimental data are currently available for the RAZOR™ Nano chamber, making this the first study to experimentally determine its k_Q values. The results obtained in this work are compared with existing data obtained through Monte Carlo simulations by González-Castaño *et al.* [126], Muir and Rogers [81] and Czarnecki and Zink [127] and experimental work from McEwen [82] in figure 4.5. The differences in k_Q values between two chambers of the same type were found to be maximally 0.2%, 0.2% and 0.1% for the RAZOR™ Nano, CC01 and CC04 chambers, respectively. The average value is presented in figure 4.5. These variations are consistent with previous studies on cylindrical ionization chambers in high-energy photon beams, which reported chamber-to-chamber differences ranging from 0.1% to 0.3% [135].

González-Castaño *et al.* [126] performed Monte Carlo simulations using the

EGSnrc system to obtain k_Q values for the CC01 and CC04 chambers across TPR_{20,10} values ranging from 0.674 to 0.8, with reported statistical uncertainties between 0.5 and 1% (excluding type B uncertainties). Muir and Rogers [81] conducted Monte Carlo simulations for the CC01, CC04 and CC08 chambers. Their polynomial fit, which has an estimated uncertainty up to 0.99%, was used for comparison in this study. Czarnecki and Zink [127] performed Monte Carlo simulations to determine the k_Q -factors for the RAZOR™ Nano, CC04 and CC08 chambers. Their polynomial fit was used to compare with the values determined in this work. The experimental data of McEwen [82] is based on cross-calibration of the chambers against a set of reference chambers, calibrated against the Canadian primary standard sealed water calorimeter [136]. The uncertainty on these values was estimated to be 0.3%. The total uncertainty on the k_Q values obtained in this work (varying between 1.07% and 1.50%) is considerably larger than the uncertainties reported on the experimental values obtained by McEwen [82]. This is mainly due to the high uncertainty of the heat transfer correction for the calorimetric measurements and the uncertainty on the calibration coefficients of the used chambers.

The only available data for the RAZOR™ Nano chamber is from the work of Czarnecki and Zink [127] and is derived from Monte Carlo simulations. Comparison of the experimental k_Q -factors obtained in this study with their polynomial fit demonstrates good agreement across the entire range of investigated beam qualities. As no historical calibration data were available for these chambers, no conclusions can be made regarding their long-term stability.

For the CC01 chamber, comparing the results obtained in this work to the other existing data revealed deviations larger than 3% for some beam qualities. A possible explanation for the lower k_Q values obtained in this work is the use of a 20 cm × 20 cm field rather than the standard 10 cm × 10 cm field. As mentioned in TRS-483 [128], if high Z materials are used in the detector's construction, detector response might change with field size. Given that the CC01 chamber features a steel central electrode, the chamber will over respond due to the photoelectric effect which results in lower k_Q values. Similar observations have been reported by Azangwe *et al.* [137]. Significant deviations in k_Q values for ion chambers using high-Z electrodes were also reported in the work of Muir and Rogers [138]. It is important to note that the data reported by Czarnecki and Zink [127] is for the IBA RAZOR™ chamber, which differs from the IBA CC01 chamber used in this work, despite having the same cavity volume and dimensions. The distinction between both chamber types lies in the composition of the electrode: the CC01 features a steel electrode, while for the RAZOR™ chamber graphite is used and therefore the k_Q -factors might differ

between these two types. The values reported by Czarnecki and Zink [127] for the RAZORTM chamber are therefore not included in figure 4.5.

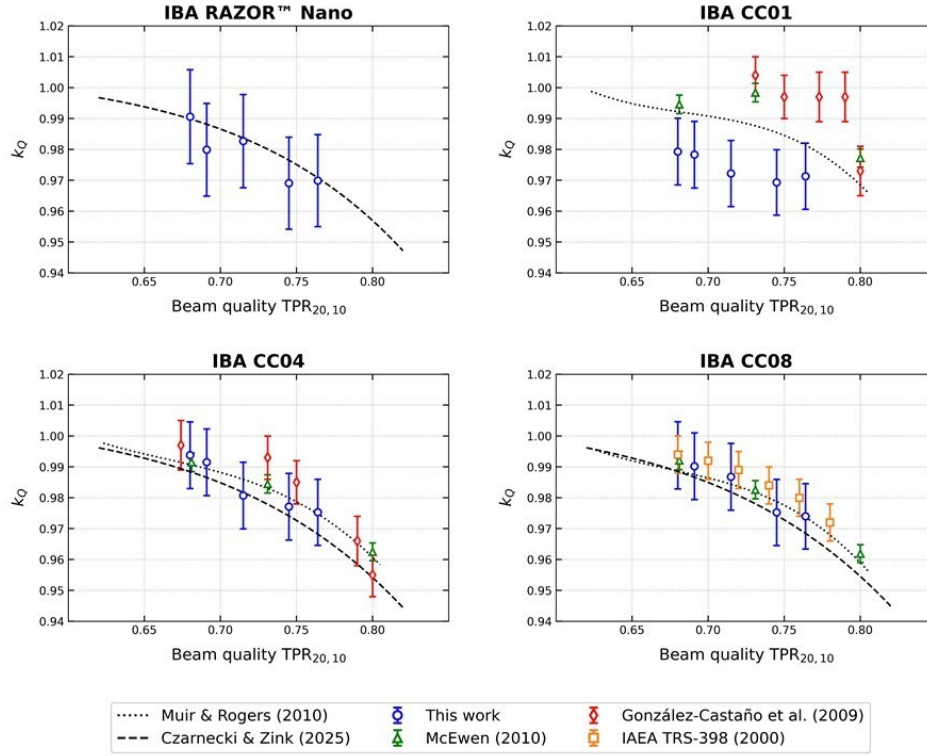


Figure 4.5: k_Q -factors in function of beam quality $TPR_{20,10}$ for the cylindrical ionization chambers (RAZORTM Nano, CC01, CC04 and CC08) in high-energy photon beams. Open circles represent the values obtained in this work through the use of our water calorimeter. Open triangles represent experimental values obtained by McEwen [82], diamonds are values obtained through Monte Carlo simulations by González-Castaño *et al.* [126], the dotted line is a fit obtained from Monte Carlo simulations by Muir and Rogers [81] and the dashed line is a fit obtained from Monte Carlo simulations by Czarnecki and Zink [127]. Squares represent values recommended in the initial version of IAEA TRS-398. Error bars represent standard uncertainties ($k = 1$).

For the CC04 chamber, good agreement is observed between the experimentally determined k_Q -factors obtained in this work and the available Monte Carlo and experimental data, with all values agreeing within their respective uncertainties. Polarity and ion recombination corrections were found to be

small and stable across the investigated beam qualities. In addition, the analysis of the calibration coefficients over multiple years demonstrates compliance with the stability criteria recommended in TRS-398 Rev. 1. Together, these findings indicate a stable and reproducible response of the CC04 chamber in high-energy photon beams.

For the CC08 chamber, values were included in the first version of IAEA TRS-398 but not in the updated version of 2024 [6], while values are given in the Addendum of AAPM's TG-51 [119]. The k_Q -factors given in this Addendum are taken from the work of Muir and Rogers [81] and are represented in the figure under the name of this work. The experimental data for the CC08 obtained in this work aligns closely with those values and also shows excellent agreement with other available data (experimental and Monte Carlo) [82, 126]. This consistent agreement across independent studies, combined with the small polarity and recombination corrections and the long-term stability of the chamber, provides confidence in the use of the CC08 chamber in high-energy photon beams.

4.5.2 Plane-parallel ionization chambers

For the PPC40 measurements, three different chambers were used, and the obtained k_Q -factors for all chambers were in good agreement across the entire range of beam qualities, with maximum deviations of 0.2%. This is consistent with the results obtained by Muir *et al.* [124], where they reported chamber-to-chamber variations in k_Q values for plane-parallel chambers of the same type to be around 0.2% for the PPC40 and 0.3% for the PPC05, using two chambers of each type. In our study, only one PPC05 chamber was used, so no conclusions can be drawn regarding chamber-to-chamber variability for this model.

Figure 4.6 shows the k_Q values obtained in this work alongside data published by Muir *et al.* [124], obtained through Monte Carlo simulations and experimental measurements. For the PPC40 chamber measurements done in this work, the average of the three chambers is presented. In the study of Muir *et al.* [124], the polynomial fit to the Monte Carlo-derived k_Q -factors was expressed in function of $\%dd(10)_x$ (the photon component of the percentage depth dose at 10 cm depth in a 10 cm $\times$ 10 cm field) instead of $TPR_{20,10}$. To be able to compare the k_Q values, their data was adapted according to the relation given in IAEA TRS-398 Rev. 1 page 84 [6]. Systematic uncertainties for the calculated k_Q -factors were in the order of 0.5%. The experimental data from their study were obtained through cross-calibration with reference chambers, which were calibrated against the NRC primary standard water calorimeter. The combined

uncertainty for the measured k_Q -factors was 0.4%.

Across the entire range of investigated beam qualities, the experimental and Monte Carlo data for the PPC05 chamber were in good agreement, with maximum deviations of approximately 0.4% between the different datasets. Similarly, all data for the PPC40 chambers is in good agreement, with the largest deviation being 0.9%.

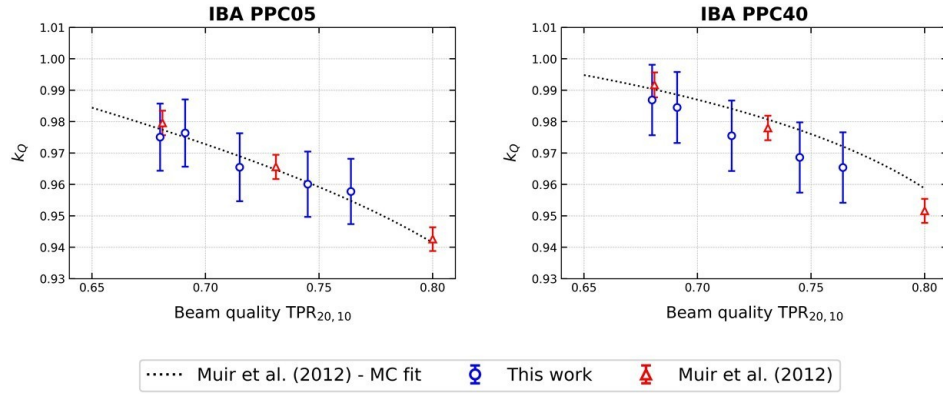


Figure 4.6: k_Q -factors in function of beam quality $TPR_{20,10}$ for plane-parallel ionization chambers (PPC05, PPC40) in high-energy photon beams. The open circles represent the values obtained in this work through the use of water calorimetry. Triangles represent experimental data obtained by Muir *et al.* [124] and the dotted line is a fit from Monte Carlo simulations obtained in the same work. Error bars represent standard uncertainties ($k = 1$).

For the plane-parallel chambers, polarity and ion recombination correction factors were small and reproducible across all beam qualities. However, long-term stability of the calibration coefficients was lower than that observed for the cylindrical chambers. Reduced stability of calibration coefficients of plane-parallel chambers has also been reported in previous studies and is one of the main reasons why such chambers are generally not recommended as reference dosimeters in high-energy photon beams [124, 139, 140]. Despite the larger variability in calibration coefficients over time, the experimentally determined k_Q -factors obtained in this work show good agreement with those obtained in the work of Muir *et al.* [124], where it has been suggested that k_Q -factors for plane-parallel chambers may be more reproducible than their calibration coefficients. According to TRS-398 Rev. 1, plane-parallel ionization chambers may be used for reference dosimetry in high-energy photon beams, provided that they have been recently calibrated and that all relevant correction factors

have been experimentally determined. In this context, the k_Q -factors may potentially be treated as generic chamber-type values, while particular care must be taken to ensure the validity of the calibration coefficient at the time of use.

4.6 Conclusion

This study evaluated the performance of several cylindrical (IBA RAZOR™ Nano, CC01, CC04, and CC08) and plane-parallel (IBA PPC40 and PPC05) ionization chamber in high-energy photon beams. Across the five different beam qualities evaluated, all chamber types demonstrated stable and consistent behavior. The polarity and recombination correction factors were found to be small and independent of beam quality. Experimentally determined beam quality correction factors, k_Q , showed strong agreement with values reported in the literature, except for the CC01 chamber, where observed discrepancies are likely due to its steel electrode. Chamber-to-chamber variations were found to be within 0.2% for all evaluated ionization chamber types. For the cylindrical chambers, calibration coefficient data available over multiple years indicated good long-term stability. For the plane-parallel chambers, larger variations in calibration coefficients were observed, consistent with findings reported in previous studies. For the IBA RAZOR™ Nano chamber, no conclusions regarding long-term stability could be drawn due to the absence of historical calibration data; however, this work provides the first experimental determination of k_Q -factors for this chamber type. Within the scope of this study, no evidence was found that would preclude the use of the CC04 and CC08 chambers as reference dosimeters in high-energy photon beams. The plane-parallel chambers investigated (PPC05 and PPC40) may be suitable for reference dosimetry provided that they are recently calibrated, in accordance with TRS-398 Rev. 1 . Further investigations involving a larger number of chambers of each type and a more comprehensive assessment of long-term stability would help to further support these conclusions.

Chapter 5

Beam quality correction factors for proton beams

The content presented in this chapter corresponds to the published article: *Experimental determination of beam quality correction factors in scanned proton beams using water calorimetry*. [Physics in Medicine and Biology, 71\(2\), 2026](#).

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5.1 Summary

Objective: To measure beam quality correction factors (k_Q) in single-layer scanned proton beams using water calorimetry for three ionization chamber types commonly used in clinical proton dosimetry.

Approach: Measurements were performed at two proton therapy centers using clinical proton beams with nominal energies of 150, 220, and 226 MeV at a reference depth of 4 cm. The k_Q -factors were obtained by comparing absorbed dose to water determinations from a water calorimeter with ionization chamber readings under identical conditions. Three ionization chamber models were investigated: the IBA FC65-G (cylindrical), PPC05 and PPC40 (plane-parallel). Two independent calorimeter setups were used across three measurement campaigns.

Main results: The measured k_Q -factors showed strong agreement with current TRS-398 Rev. 1 (2024) recommendations and literature data. For the FC65-G chamber, excellent alignment was observed with previous water calorimetry-based measurements. For the PPC40 chamber, both chambers yielded consistent results within 0.5% of TRS-398 Rev. 1. For the PPC05 chambers, a maximum deviation of 1.4% was observed relative to TRS-398 Rev. 1, and inter-chamber variability was within 0.5%. The use of two calorimeter setups yielded consistent results within 0.2%, supporting their validity.

Significance: This study presents new experimental k_Q -factors for ionization chambers in single-layer scanned proton beams, contributing to the currently scarce experimental database, providing further validation of the TRS-398 Rev. 1 (2024) recommendations, and supplying benchmark data for future Monte Carlo-based k_Q calculations.

5.2 Introduction

Accurate determination of absorbed dose to water is crucial in proton therapy for ensuring precise treatment delivery and optimal patient outcomes. Based on the $N_{D,w}$ -formalism recommended in IAEA TRS-398 Rev. 1 Code of Practice [6], the absorbed dose to water ($D_{w,Q}$) is determined using ionization chambers according to the following equation:

$$D_{w,Q}^{ion} = M_Q N_{D,w,Q_0} k_{Q,Q_0} \quad (5.1)$$

where M_Q represents the chamber reading corrected for temperature and pressure, polarity, and recombination effects, N_{D,w,Q_0} is the calibration coefficient of the chamber obtained in a reference beam of quality Q_0 and k_{Q,Q_0} is the beam quality correction factor, accounting for the differences between the reference beam and the clinical beam of quality Q . When the reference beam is ^{60}Co , the notation is simplified to k_Q , which will be used throughout this work.

The recent update of IAEA TRS-398 [6] provides k_Q -factors for a wide range of ionization chambers, based on the work of Palmans *et al.* [141], representing the current best estimates of beam quality correction factors in clinical proton beams. These values are derived from a combination of Monte Carlo simulations and experimental data. While the available Monte Carlo-based data covers a wide range of ionization chamber models [83–89], experimentally derived k_Q -factors in proton beams remain limited.

Earlier experimental determinations were limited to a small set of chambers. Vatnitsky *et al.* [91] reported k_Q -factors for two cylindrical chambers, while Palmans *et al.* [142] provided data for three plane-parallel chambers through comparison with calorimetry. Medin *et al.* extended this work focusing on Farmer-type chambers such as IBA FC65-G and NE2571 [94, 95, 97]. Additional calorimetry data was published by Sarfehnia *et al.* [143] and Gagnebin *et al.* [144], from which k_Q -factors could be extracted. Indirect measurements, based on comparison with different ionization chambers were reported by Palmans *et al.* [92, 93] and Gomà *et al.* [96], but again for a limited set of chambers.

Recently, Wang *et al.* [145] published a broader set of water calorimetry-based k_Q -factors, including values for ionization chambers not previously characterized experimentally. Their measurements were performed at 10 cm depth in single-layer beams and in the center of a spread-out Bragg peak (SOBP).

In contrast, this present study aims to experimentally determine k_Q -factors in single-layer proton beams at the reference depth of 4 cm in the plateau region, which is closer to the reference conditions prescribed by TRS-398 Rev. 1 for pencil beam scanned proton beams. Using water calorimetry, we determine k_Q -factors for two plane-parallel ionization chamber models (IBA PPC05 and PPC40) and one cylindrical model (IBA FC65-G), including multiple chambers of each type. By directly comparing calorimetric dose measurements with ionometric data, this study provides valuable experimentally determined k_Q -factors, aiming to enhance the accuracy and reliability of dosimetry in proton therapy.

5.3 Materials and methods

5.3.1 Irradiation fields

The measurements were performed during different campaigns at the Trento Proton Therapy Center (Italy) and at the MedAustron Ion Therapy Center (Austria). All measurements were performed using a field size of 10 cm × 10 cm and at a water-equivalent measurement depth of 4 cm instead of the recommended 2 cm due to the design of the calorimeter and vessel. At the Trento Proton Therapy Center, measurements were performed using two single-layer scanned proton beams (with nominal energies of 150 MeV and 226 MeV) produced by a cyclotron. The fields were delivered in one single scan of 41 × 41 spots, with the same number of Monitor Units (MU) per spot and a spot spacing of 2.5 mm. The complete field was delivered in less than 10 s. MedAustron is a synchrotron-based Ion Beam Therapy and research center, providing different particle types [146]. A single-layer scanned proton beam was used with a nominal energy of 220 MeV. 50 × 50 spots were delivered with a spot spacing of 2 mm. The delivery of the whole field took approximately 90 s, with spill lengths of 1 s.

5.3.2 Experimental determination of k_Q

Water calorimetry is considered as the most direct method to determine absorbed dose to water by measuring the irradiation induced temperature rise according to the following formula:

$$D_{w,Q}^{cal} = c_w \Delta T k \quad (5.2)$$

where c_w is the specific heat capacity of water (4204.8 J kg⁻¹ K⁻¹) at 4 °C [131],

ΔT the temperature rise due to the irradiation, and k the product of correction factors, as outlined below in section 5.3.3.

Given that absorbed dose to water obtained through calorimetry and ionometry should be equivalent, it can be stated that:

$$D_{w,Q}^{cal} = D_{w,Q}^{ion} = M_Q N_{D,w,Q_0} k_Q \quad (5.3)$$

Therefore, k_Q -factors can be determined according to the following relation:

$$k_Q = \frac{D_{w,Q}^{cal}}{M_Q N_{D,w,Q_0}} \quad (5.4)$$

This approach was used in the work of Medin *et al.* [95, 97] in proton beams and is also the approach used in this work.

5.3.3 Calorimetric determination of absorbed dose to water

The water calorimeter setup

The water calorimeter used in this work was designed based on the water calorimeter operated at McGill University. A detailed description of the water calorimeter and its components can be found in the works of Sarfehnia [105] and Renaud [106]. For a brief overview, the water calorimeter consists of a 30 cm × 30 cm × 30 cm water tank constructed from polymethyl methacrylate (PMMA), surrounded by layers of polystyrene for thermal insulation. The calorimeter is maintained at a stable temperature of 4 °C using an internal heat exchanger connected to an external fridge to minimize convective heat transfer within the water. The water tank has a horizontal entrance window made out of PMMA with a thickness of 1 mm. The core of the detector is a plane-parallel glass vessel (figure 5.1 (a)) which is positioned inside the water tank. Two thermistor probes are positioned inside this vessel with an inter-probe distance of 2 mm using a traveling microscope. Each probe contains a thermistor bead with a nominal resistance of 10 kΩ at 4 °C. The two thermistor probes are connected to an AC bridge and the voltage output is converted into temperature through calibrations. More detailed descriptions of the electronic circuit and calibrations can be found in the following references [105–107].

Two calorimeter setups were employed across the measurement campaigns, differing primarily in the geometry of the vessel and the distance between the

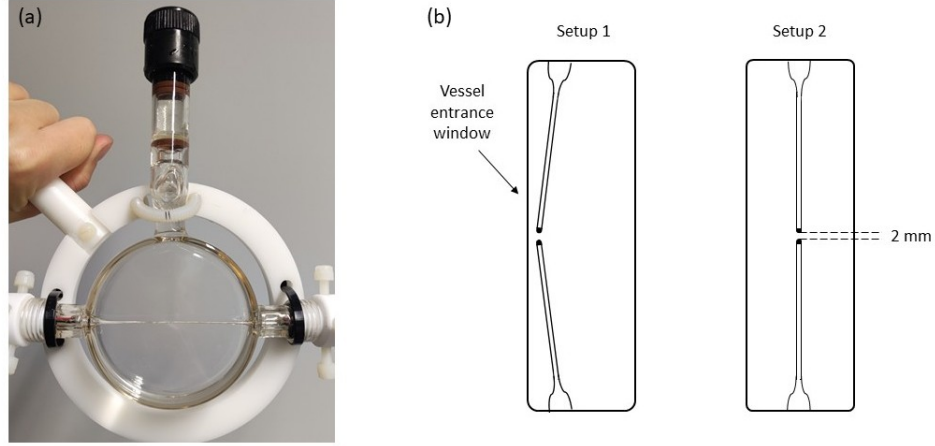


Figure 5.1: (a) Picture of the plane-parallel glass vessel with the two thermistor probes inside. (b) Graphical representation of the two setups, highlighting their difference regarding the probe-to-window distances.

thermistor probes and the vessel entrance window. Setup 1, used during the first campaign in Trento and for all measurements at MedAustron, involved a vessel with a diameter of 7.9 cm, a height of 2.36 cm, and a 1.12 mm thick entrance window. Setup 2, used during the final measurements in Trento, utilized a vessel with a diameter of 8.02 cm, a height of 2.77 cm, and a thinner 0.7 mm entrance window. The key distinction between the two setups is illustrated in figure 5.1 (b) and lies in the probe-to-window distance. This distance significantly influences the heat transfer towards the thermistor probes and, consequently, the heat transfer correction factor, which is discussed further in sections 5.3.3 and 5.4.1. The vessel of setup 1 was originally designed for low-energy electron beams, where space constraints were important.

Correction factors

As introduced in equation 5.2, several correction factors need to be applied to the response of the calorimeter:

$$k = k_c k_p k_{dd} k_\rho k_{HD} \quad (5.5)$$

The correction factor k_c corrects for the conductive heat transfer inside the calorimeter due to the irradiation of the glass vessel and thermistor probes

as well as variations in the local dose profile. It is defined as the ratio of the ideal temperature rise in the absence of conduction to the actual temperature rise observed in the presence of conduction. To evaluate this correction, finite element simulations were performed simulating the conductive heat transfer inside the water calorimeter using the COMSOL Multiphysics software (version 6.0). A 3D model of the water tank, including the glass vessel and thermistor probes was created to replicate the experimental setup. The dose distribution inside the water phantom is implemented as a time-dependent heat source with the same timing as during the measurements. The longitudinal dose profile was derived from percentage depth dose (PDD) profiles, while a laterally homogeneous dose distribution was assumed based on the work of Sarfehnia *et al.* [143] and Sassowsky & Pedroni [147]. Figure 5.2 illustrates the differences in beam delivery between the two proton therapy centers. For the measurements performed at the Trento Proton Therapy Center, where the beam is generated by a cyclotron, it was assumed that the entire field was delivered at once due to the rapid delivery time compared to the heat conduction coefficient of water, as was also done by Holm *et al.* [98]. This approximation is expected to have a negligible impact on the resulting k_c value relative to the overall uncertainty of the correction factor. In contrast, for the data obtained at MedAustron, where the beam is produced by a synchrotron and delivered in discrete spills separated by breaks, the temporal structure of the beam was considered in the heat transfer model. An average spill/break sequence was simulated, in which all the spots within each spill were assumed to be delivered simultaneously as was also done in the work of Holm *et al.* [98]. For the analysis of the data, the same numbers of consecutive runs and the same pre- and post-drift intervals were considered as during the measurements.

As the water calorimeter is operated at 4 °C, convective heat transfer inside can be neglected [108].

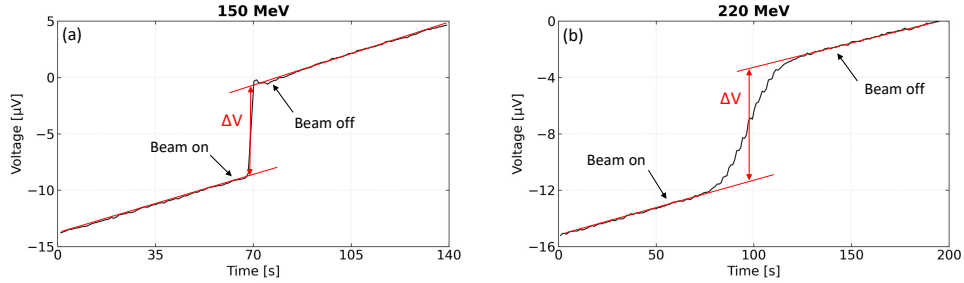


Figure 5.2: Output signal of the AC bridge for the measurements performed in (a) the 150 MeV proton beam at the Trento proton Therapy Center and (b) in the 220 MeV proton beam at MedAustron Ion Therapy Center. The pre- and post-drift curves are linearly extrapolated (red lines) to the mid-irradiation time to obtain the voltage change (ΔV) induced by the irradiation.

To account for the perturbation introduced by the presence of the glass vessel, the correction factor k_p is applied. This correction factor is defined as the ratio of the dose at the thermistor location in an idealized geometry (i.e., with the vessel and probe materials replaced by water) to the dose at the same location in the actual geometry, which includes the glass vessel and thermistor probes. This correction is determined through Monte Carlo simulations using GATE/Geant4 (v9.0, physics list QGSP BIC HP). A 3D model of the calorimeter is implemented, incorporating the geometry of the vessel and a simplified representation of the thermistor probes. The dose is scored in a small volume corresponding to the position of the thermistor beads. Two simulations are carried out: one with the true material composition and one with all non-water materials substituted with water, allowing for the computation of k_p as the ratio of these dose values. Simulations were run until a statistical uncertainty below 0.05% on the dose values is reached.

To account for non-uniformities of the lateral dose profile, correction factor k_{dd} is introduced. As the thermistor beads are positioned 1 mm either side of the central axis, and due to the flat dose profiles around the central axis of a $10 \text{ cm} \times 10 \text{ cm}$ scanned proton field, this correction was taken to be unity with an associated uncertainty of 0.20%. This uncertainty was estimated by evaluating k_{dd} for different thermistor positions varying $\pm 1 \text{ mm}$ in every orthogonal direction based on lateral dose profiles obtained either from a Lynx detector (IBA Dosimetry) or from the beam model of the treatment planning system (RayStation, RaySearch Laboratories).

The correction factor k_p accounts for the difference in water density between the temperatures at which calorimetric and ionometric measurements are performed. Specifically, water calorimetry is conducted at 4 °C, whereas ionization chamber measurements are carried out at a room temperature of about 20 °C. This temperature-dependent density variation leads to a slight difference in the effective measurement depth. By knowing the density of water at the different temperatures and the depth-dose distributions of the different beams, the correction factor can be derived. Since all measurements in this study were performed in the plateau region of the proton beam, where the dose gradient is minimal, the impact of this depth shift is negligible. Consequently, the determined correction factors were 0.9998 for 150 MeV and 0.9999 for 220 MeV and 226 MeV.

The correction factor k_{HD} accounts for the heat defect, which refers to the discrepancy between the energy absorbed from the radiation and the energy appearing in the form as heat. This effect is caused by endo- and exothermic chemical reactions due to the radiolysis of water and the presence of impurities in the water. Detailed modeling of radiation-induced chemical reactions in various aqueous systems was carried out by Klassen & Ross [116], who demonstrated that when ultrapure water is saturated with hydrogen and subjected to pre-irradiation, a chemical steady state is achieved. Under these conditions, the net heat defect is zero. Based on the findings of Krauss [132], a heat defect correction factor of unity can be assumed in such a system, with an associated uncertainty of 0.14%. While most of this work was focused on low-LET radiation, Sassowsky & Pedroni [147] confirmed that this zero heat defect was also valid in higher LET radiation. This system was successfully used in proton beams by Palmans *et al.* [148], Sarfehnia *et al.* [143], and Wang *et al.* [145], with an associated uncertainty of 0.3%. Since the calorimeter vessel in the present study was prepared using the same conditions, the same correction factor and uncertainty are adopted.

5.3.4 Ionometry

Two types of plane-parallel ionization chambers were used: three IBA PPC05 chambers (#475, #752 and #1591), with an electrode spacing of 0.6 mm and collecting electrode diameter of 10 mm, and two IBA PPC40 chambers (#508 and #512), with an electrode spacing of 2 mm and collecting electrode diameter of 16 mm. In addition, one Farmer-type cylindrical ionization chamber (IBA FC65-G #516) was used. All ionization chamber measurements were performed under the same experimental conditions as the water calorimetry measurements, with the chambers positioned inside the water calorimeter in dedicated holders

and the water at room temperature. Positioning of the ionization chambers followed IAEA TRS-398 Rev. 1 recommendations: plane-parallel chambers were aligned such that the inner surface of the entrance window corresponded to the measurement depth (considering the water-equivalent thickness (WET)), while the cylindrical chamber was positioned with its central electrode (reference point) at the desired depth. The ionization chamber readings were corrected for temperature and pressure, polarity and recombination effects. The recombination correction factor k_s was determined using the two-voltage method as described in the TRS-398 Rev. 1 protocol. Recombination and polarity corrections were measured for one chamber of each type and assumed to be the same for all chambers of the same type.

The ionization chambers were operated at the voltage for which the N_{D,w,Q_0} -values were obtained. Table 5.1 summarizes the applied voltage, the corresponding N_{D,w,Q_0} coefficients, and their associated uncertainties ($k=1$). As shown, the uncertainty on the calibration coefficient is 0.5% for all chambers except the FC65-G. The higher uncertainty (1.1%) corresponds to factory calibrations performed at IBA Dosimetry, while the lower uncertainty (0.5%) corresponds to calibrations carried out at the Secondary Standard Dosimetry Laboratory (SSDL) of IBA Dosimetry, traceable to the PTB Primary Standard Dosimetry Laboratory (Germany). All calibrations were carried out in accordance with the TRS-398 Rev. 1 code of practice.

Chamber	Voltage (V)	N_{D,w,Q_0} (Gy/C)	Uncertainty (%)
PPC05 #475	-300	5.846×10^8	0.5
PPC05 #752	+300	5.871×10^8	0.5
PPC05 #1591	-300	5.909×10^8	0.5
PPC40 #508	-300	8.212×10^7	0.5
PPC40 #512	-300	8.172×10^7	0.5
FC65-G #516	+300	4.817×10^8	1.1

Table 5.1: Overview of the used ionization chambers, their operating voltage, ^{60}Co calibration coefficient, and associated uncertainty ($k = 1$).

5.3.5 Overview of measurement campaigns

For clarity, an overview of the different measurement campaigns with the used experimental conditions and ionization chambers is given in table 5.2. Since the calorimeter vessel is reassembled before each measurement campaign, the

exact positioning of the thermistor probes varies slightly between campaigns, even when using the same vessel.

	Campaign 1	Campaign 2	Campaign 3
Proton center	Trento	MedAustron	Trento
Calorimeter setup	1	1	2
Probe–window distance	4.2 mm	3.4 mm	12.8 mm
Beam energy (MeV)	150, 226	220	226
Ionization chambers	PPC05 #475	PPC05 #475	PPC05 #475
	PPC40 #512	PPC05 #1591	PPC05 #752
		FC65-G #516	PPC05 #1591
			PPC40 #508
			PPC40 #512

Table 5.2: Overview of the different measurement campaigns. For inter-campaign comparison, the PPC05 #475 was measured in all campaigns.

5.4 Results

5.4.1 Calorimetry

The correction factors applied to the calorimeter output are summarized in table 5.3. The most notable difference between the two calorimeter setups was observed in the heat transfer correction factor (k_c). Due to the shorter probe-to-window distance in setup 1, conductive heat transfer is more significant, leading to correction factors of up to 10%. In contrast, the larger distance in setup 2 results in a smaller heat transfer correction closer to 1%. As expected, this also affects the associated uncertainty: higher heat transfer corrections lead to larger uncertainties on the final dose determination. The dominant source of this uncertainty is the positioning of the thermistors within the vessel. Even a slight misalignment can substantially alter the correction factor for the probes located near the window, whereas the same deviation has a much smaller effect for the probes positioned in the center of the vessel. The total uncertainty budget for the calorimetric determination of absorbed dose to water is provided in table 5.4. All uncertainty estimations are in accordance with the work of Lechner & Palmans [149]. For all other corrections, values were consistent across energies and setups, with negligible impact on the final results.

Beam energy	k_c	k_p	k_ρ	k_{dd}	k_{HD}
150 MeV	0.9233 (1)	0.9976 (1)	0.9998	1.000	1.000
220 MeV	0.8906 (1)	0.9983 (1)	0.9999	1.000	1.000
226 MeV	0.9215 (1)	0.9985 (1)	0.9999	1.000	1.000
	0.9909 (2)	0.9991 (2)			

Table 5.3: Correction factors applied to the calorimeter output. The numbers in parentheses refer to calorimeter setup 1 or 2. If no number is given, the correction factor was used for both setups.

Between 25 and 30 irradiations were performed for each energy to achieve a relative standard uncertainty of 0.2% on the measured temperature rise, demonstrating the calorimeter's stability. In addition to the uncertainties on the calorimeter output and correction factors, contributions from the specific heat capacity of water (0.05%, [95]), thermistor sensitivity, calibrations, and positioning are also included in the total uncertainty budget. The combined effect of these sources results in a total uncertainty of 0.93% (setup 1) and 0.57% (setup 2) on the calorimetric determination of absorbed dose to water.

Quantity	Relative standard uncertainty (%)
Temperature rise ΔT	0.2
Specific heat capacity c_w	0.05
Calibrations	0.2
Thermistor sensitivity	0.07
Positioning	0.08
Heat transfer correction k_c	0.8 (1) / 0.3 (2)
Beam perturbation correction k_p	0.1
Density correction k_ρ	0.01
Dose profile non-uniformity k_{dd}	0.2
Heat defect k_{HD}	0.3
$D_{w,Q}^{cal}$	0.93 (1) / 0.57 (2)

Table 5.4: Uncertainty budget for absorbed dose to water ($D_{w,Q}^{cal}$) obtained through water calorimetry. The numbers in parentheses refer to the calorimeter setup used.

5.4.2 Ionometry

All ionization chamber measurements were conducted under the same irradiation conditions as the calorimetry measurements. A total of 10 repeated readings were taken per voltage for each ionization chamber. Raw ionization chamber readings were corrected for temperature and pressure, polarity, and ion recombination in accordance with TRS-398 Rev. 1. The applied polarity and recombination corrections are given in table 5.5 for each chamber type. Polarity corrections were measured in a single beam and assumed to be independent of the beam delivery and energy. For the PPC05 and PPC40 chambers, which were used both at Trento and MedAustron, recombination corrections were measured under both beam conditions. The small values of the corrections justify that they have been measured only for one chamber of each type.

	FC65-G	PPC05	PPC40
k_{pol}	0.9999	1.0006	1.0004
k_s	1.0009	1.0012 (Trento)	1.0025 (Trento)
		1.0008 (MedAustron)	1.0003 (MedAustron)

Table 5.5: Polarity and recombination correction factors applied to the different ionization chambers.

The correction for field non-uniformity at the ionization chamber position was assumed to be unity, with an associated standard uncertainty of 0.2%, consistent with the approach used for the calorimeter's lateral correction. To estimate the total uncertainty on M_Q , the uncertainties related to the uncorrected signal, correction factors and chamber positioning were combined. This yielded a combined standard uncertainty of 0.31% ($k = 1$) for M_Q .

5.4.3 k_Q -factors

The k_Q -factors were determined according to equation 5.4 and are given in table 5.6. The setup used for each measurement is indicated in parentheses. The combined standard uncertainty ($k=1$) on the k_Q -factors was calculated as the square root of the sum of the squared individual contributions ($D_{w,Q}^{cal}$, M_Q and N_{D,w,Q_0}). The total uncertainties varied between 0.82% and 1.48%, depending on the used calorimeter setup and ^{60}Co calibration coefficient.

Chamber	150 MeV	220 MeV	226 MeV
PPC05 #475	1.005(11) (1)	1.003(11) (1)	1.003(11) (1) 1.005(8) (2)
PPC05 #752	–	–	1.002(8) (2)
PPC05 #1591	–	0.999(11) (1)	1.000(8) (2)
PPC40 #508	–	–	0.989(8) (2)
PPC40 #512	0.989(11) (1)	–	0.991(11) (1) 0.990(8) (2)
FC65-G #516	–	1.021(15) (1)	–

Table 5.6: k_Q -factors obtained for the different chambers during the three measurement campaigns. The values in parentheses represent the relative standard uncertainty on the last digits. (1) refers to setup 1 and (2) to setup 2.

5.5 Discussion

The measurements presented in this work were performed using two distinct experimental setups (two different vessels), as described in Section 5.3.3. Although setup 1 required a larger heat transfer correction, the resulting k_Q -factors are in good agreement with those obtained using setup 2. Both setups were operated under identical conditions in a 226 MeV clinical proton beam. The observed differences in the resulting k_Q -factors were within 0.2% for the PPC05 #475 chamber and below 0.05% for the PPC40 #512 chamber. This demonstrates the consistency between the two setups and confirms the high accuracy of the calculated conductive heat transfer correction factor despite the large value of the correction for setup 1. However, due to the larger associated uncertainties, setup 1 is considered less optimal for high-precision measurements.

The k_Q -factors obtained in this work for the three ionization chamber types (FC65-G, PPC05, and PPC40) were compared to both experimental and Monte Carlo data available in the literature. For the PPC05 and PPC40 chambers, the only experimental data are those reported by Wang *et al.* [145], based on water calorimetry measurements. The primary distinction from the experimental data reported by Wang *et al.* [145] is in the measurement conditions. While their measurements were performed either at the center of a spread-out Bragg peak (SOBP) or at a reference depth of 10 cm in single-layer scanned beams, all measurements in the present work were conducted in single-layer scanned proton beams at a reference depth of 4 cm, more closely matching the reference conditions of TRS-398 Rev. 1. Monte Carlo-based k_Q values have been published

by Gomà *et al.* [83], Gomà & Sterpin [86], and Baumann *et al.* [87, 89]. A comparison of these datasets with the present measurements and the TRS-398 Rev. 1 (2024) recommendations is shown in figures 5.3, 5.4 and 5.5. The deviations between the data obtained in this work and the TRS-398 Rev. 1 recommendations are presented in table 5.7.

The standard uncertainties of the k_Q -factors obtained in this work are slightly larger than those reported by Wang *et al.* [145]. While the uncertainties associated with the calorimetric absorbed dose to water $D_{w,Q}^{cal}$ and the corrected ionization chamber reading M_Q are of similar magnitude in both studies (approximately 0.5% and 0.3%, respectively), the dominant difference arises from the calibration coefficient N_{D,w,Q_0} . In the work of Wang *et al.* [145], calibration coefficients were obtained using a primary standard water calorimeter, achieving a relative standard uncertainty of 0.26%. In contrast, the calibration coefficients used in this present work were provided by the IBA Dosimetry SSDL, as described in section 5.3.4, resulting in a slightly higher overall uncertainty.

Chamber	150 MeV	220 MeV	226 MeV
PPC05 #475	1.36% (1)	1.20% (1)	1.20% (1) 1.38% (2)
PPC05 #752	–	–	1.07% (2)
PPC05 #1591	–	0.79% (1)	0.89% (2)
PPC40 #508	–	–	-0.52% (2)
PPC40 #512	-0.53% (1)	–	-0.35% (1) -0.40% (2)
FC65-G #516	–	0.01% (1)	–

Table 5.7: Difference between the experimentally determined k_Q -factors in this work and the TRS-398 Rev. 1 (2024) recommendations. (1) refers to setup 1 and (2) to setup 2.

For the FC65-G cylindrical chamber, several experimental k_Q values have been reported in the literature. Measurements by Medin *et al.* [94, 97] and Wang *et al.* [145] were obtained via direct comparison with a water calorimeter, while those by Gomà *et al.* [96] used a cross-calibration approach. The k_Q value obtained in this work is in excellent agreement with the TRS-398 Rev. 1 (2024) recommendation, and also aligns closely with other experimental data at a similar residual range [97]. This provides additional experimental validation of the TRS-398 Rev. 1 curve for this chamber.

For the PPC05 plane-parallel chamber, three different serial numbers (#475,

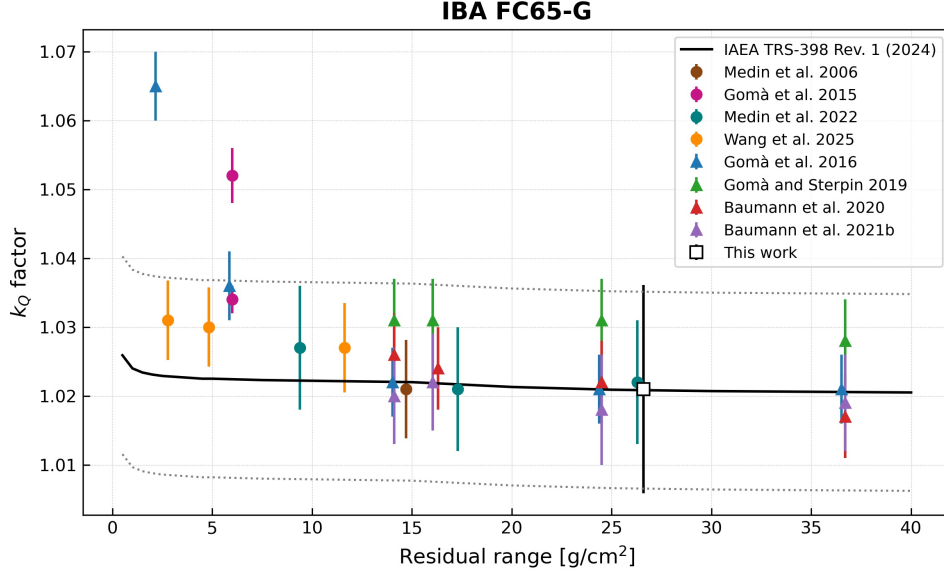


Figure 5.3: k_Q -factors for the IBA FC65-G chamber as function of residual range. The plot compares the data recommended in TRS-398 Rev. 1 [6], experimental data (circles) available in literature [94, 96, 97, 145] and data obtained through Monte Carlo simulations (triangles) [83, 86, 87, 89] with the value obtained in this work (square). The dotted lines indicate the standard uncertainty ($k = 1$) on the TRS-398 Rev. 1 values. All uncertainty bars associated with individual data points represent standard uncertainties ($k = 1$).

#752, and #1591) were evaluated during multiple measurement campaigns. Overall, the results agree with the TRS-398 Rev. 1 (2024) recommendations, although the values obtained in this work are systematically higher. The smallest deviation was observed for chamber #1591 ($\approx 0.8\%$), while the largest was found for chamber #475, reaching up to 1.4%. The experimental data reported by Wang *et al.* [145] (0.993 – 0.994) show closer agreement with the TRS-398 Rev. 1 values. The k_Q -factors obtained with the three different PPC05 chambers agree within the stated uncertainties. However, a reproducible difference of approximately 0.5% is observed between chambers #1591 and #475 across multiple measurement campaigns, with chamber #752 yielding intermediate values.

It should be noted that the positioning of plane-parallel ionization chambers can influence the derived k_Q values. In this work, the water-equivalent thick-

ness of the entrance window was considered when positioning the ionization chambers, as recommended in TRS-398 Rev. 1. However, this WET shift is typically not included in Monte Carlo simulations, which may partly explain the observed differences [150]. The work of Baumann *et al.* [150] showed that this effect is generally small when dose-gradients are small (as for the energies used here), but for the PPC05 chamber this may lead to differences of up to 0.5% on the k_Q -factors presented in TRS-398 Rev. 1.

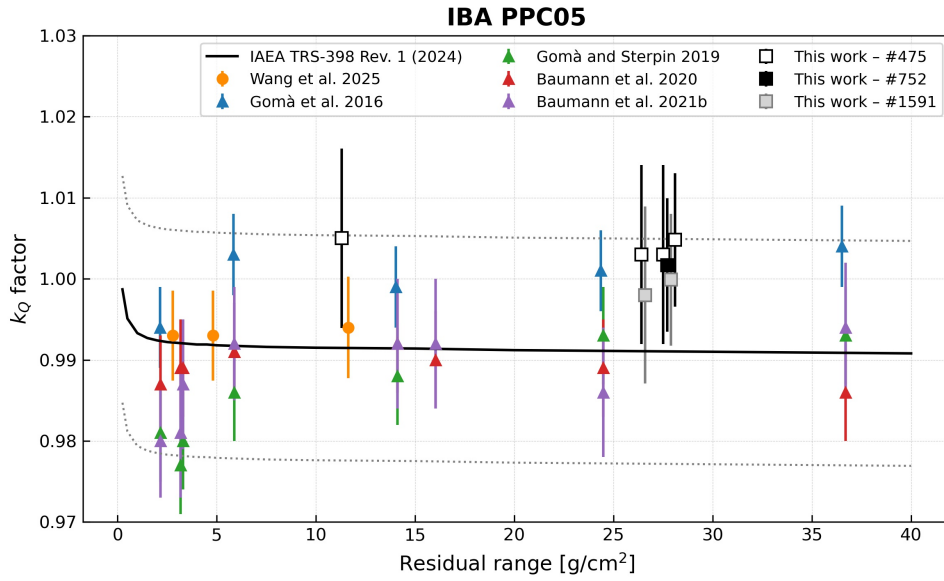


Figure 5.4: k_Q -factors for the IBA PPC05 chamber as function of residual range. The plot compares the data recommended in TRS-398 Rev. 1 [6], experimental data (circles) by Wang *et al.* [145] and k_Q -factors obtained through Monte Carlo simulations (triangles) [83, 86, 87, 89] with the values obtained in this work (square). The values obtained in this work with the same residual range are shifted ± 0.2 g/cm² for better visibility. The dotted lines indicate the standard uncertainty ($k = 1$) on the TRS-398 Rev. 1 values. All uncertainty bars associated with individual data points represent standard uncertainties ($k = 1$).

For the PPC40 chamber, two different serial numbers (#508 and #512) were assessed. Both yielded k_Q -factors that were slightly lower than the TRS-398 Rev. 1 values but are in good agreement with most available Monte Carlo data. Although the value determined in this study agrees with that of Wang *et al.* [145] within the stated uncertainties for a similar residual range, a discrepancy

of 1.4% was observed. Importantly, the two chambers used in this work exhibit excellent agreement. However, given that their serial numbers are close, it is likely they originate from the same manufacturing batch, which may limit the observed variability.

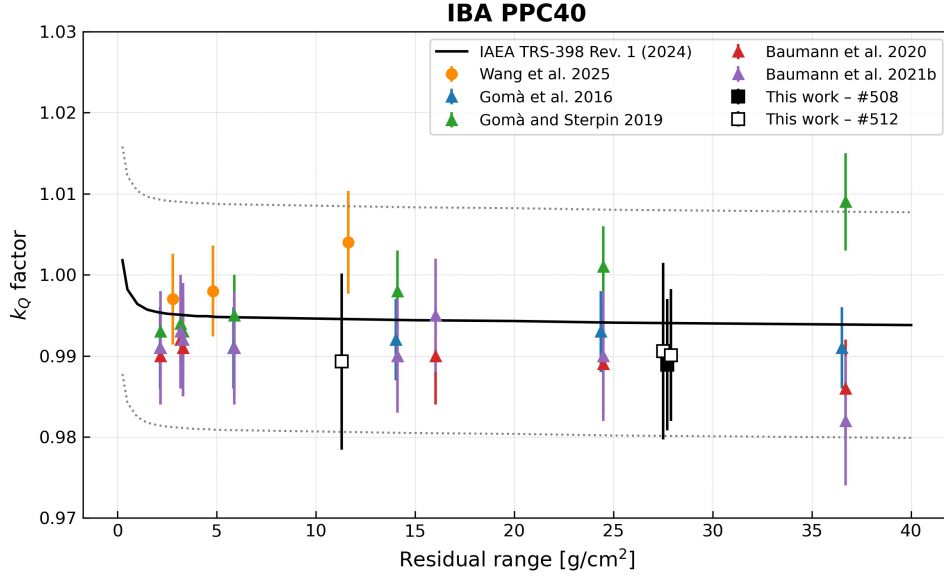


Figure 5.5: k_Q -factors for the IBA PPC40 chamber as function of residual range. The plot compares the data recommended in TRS-398 Rev. 1 [6], experimental data (circles) by Wang *et al.* [145] and k_Q -factors obtained through Monte Carlo simulations (triangles) [83, 86, 87, 89] with the values obtained in this work (square). The values obtained in this work with the same residual range are shifted ± 0.2 g/cm² for better visibility. The dotted lines indicate the standard uncertainty ($k = 1$) on the TRS-398 Rev. 1 values. All uncertainty bars associated with individual data points represent standard uncertainties ($k = 1$).

5.6 Conclusion

Beam quality correction factors were experimentally determined for the FC65-G, PPC05, and PPC40 ionization chambers in clinical scanned proton beams using two independent calorimetry setups. Despite differences in heat transfer corrections, both setups yielded consistent results under identical conditions, with deviations below 0.2%, confirming their reliability. The measured k_Q -factor for the FC65-G chamber agrees closely with the recommendations of TRS-

398 Rev. 1 (2024) and previous calorimetry-based studies, thereby supporting the recommendations as well as the method used in this work. Three serial numbers were investigated for the PPC05 chamber. While all results were generally consistent with TRS-398 Rev. 1 and Monte Carlo data, differences of up to 1.4% were observed for one chamber, and an inter-chamber variability of approximately 0.5% was identified. In contrast, PPC40 measurements from two chambers showed excellent agreement with each other, TRS-398 Rev. 1, and literature data. Overall, the data presented in this study provide strong experimental support for the k_Q values currently recommended in TRS-398 Rev. 1 for the three types of ionization chambers studied here. In addition, this work provides high-quality benchmark data for future Monte Carlo-based k_Q calculations, highlighting the importance of consistent ionization chamber positioning in both experimental measurements and Monte Carlo simulations.

Chapter 6

Beam quality correction factors for carbon and helium ion beams

The content presented in this chapter corresponds to a manuscript titled: *Water calorimetry-based beam quality correction factors for carbon and helium ion beams*, which has been submitted to Physics in Medicine and Biology.

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6.1 Summary

Objective: To determine beam quality correction factors, k_Q , in single-layer scanned carbon and helium ion beams using water calorimetry, thereby reducing uncertainties in dosimetry for light ion therapy.

Approach: Water calorimetry measurements were performed under harmonized conditions at two synchrotron-based ion beam therapy centers (MedAustron, Austria and HIT, Germany). Measurements were conducted in the plateau region of single-layer scanned beams. Carbon ion beams covered nominal energies from 213.4 to 402.8 MeV/u, while helium ion beams were measured at 196.3 and 198.8 MeV/u. Multiple cylindrical (IBA FC65-G, PTW 30013) and plane-parallel (IBA PPC05, PPC40; PTW 34001, 34045) ionization chamber types were investigated.

Main results: k_Q -factors were determined with standard uncertainties of approximately 1%, depending on chamber type and measurement condition. For all investigated chambers, inter-center agreement was observed within the combined standard uncertainties. Chamber-to-chamber variability was below 0.5% for chamber types for which two samples were available, except for the IBA PPC05, for which differences up to 1.3% were observed. For carbon ion beams, the measured k_Q -factors are consistent with previously published water calorimetry-based results. However, systematic deviations up to 3% persist between experimentally determined and Monte Carlo-derived k_Q values. The measured k_Q -factors for helium ions show trends that are broadly similar to those observed in carbon ion beams across all chamber types.

Significance: This work expands the experimental k_Q -database for light ions by providing new carbon ion data and the first experimental k_Q -factors for helium ion beams. These results provide essential experimental data for future refinement of dosimetry recommendations, and highlight persistent discrepancies between the experimental and Monte Carlo-based k_Q -factors that require further investigation.

6.2 Introduction

Proton and ion beam therapy offer distinct physical and biological advantages over conventional radiotherapy, potentially enabling more effective tumor control with improved normal-tissue sparing [151, 152]. Proton therapy is now widely established, whereas light ion beam therapy, including carbon and helium ions, remains less available, yet offers potential benefits over protons in selected cases. Carbon ions exhibit a higher linear energy transfer (LET) than protons and consequently a higher relative biological effectiveness (RBE), which is preferable for treating radioresistant tumors [27, 40]. Helium ions exhibit physical and biological properties that fall between those of protons and carbon ions. Compared to protons, helium ion beams exhibit reduced lateral scattering and range straggling together with an increase in RBE [42, 45–47]. Relative to carbon ions, they preserve a sharp lateral penumbra while introducing less nuclear fragmentation and lower radiobiological uncertainty [48, 49, 153], making helium ions an advantageous modality for pediatric treatments. Despite these advantages, helium ion therapy is not yet established in routine clinical use, and only a few patients have been treated so far with modern delivery techniques [43, 44].

An important remaining challenge in light ion beam therapy is the establishment of accurate reference dosimetry. Following the TRS-398 Rev. 1 Code of Practice (CoP) [6], the determination of absorbed dose-to-water in light ion beams using ionization chambers (ICs) has a combined standard uncertainty of 2.6-2.7%, depending on the chamber type, compared to 1% for high-energy photons and 1.7% for protons. This high uncertainty is dominated by the beam quality correction factor k_{Q,Q_0} . This k_{Q,Q_0} -factor is applied to correct for the different response of the ionization chamber at the user beam quality Q relative to the reference beam quality Q_0 (used to calibrate the IC). In TRS-398 Rev. 1, k_{Q,Q_0} -factors for light ion beams are derived from theoretical calculations according to the following equation:

$$k_{Q,Q_0} = \frac{(s_{w,air})_Q (W_{air})_Q p_Q}{(s_{w,air})_{Q_0} (W_{air})_{Q_0} p_{Q_0}} \quad (6.1)$$

where $s_{w,air}$ is the stopping power ratio, W_{air} the mean excitation energy per ion pair and p the chamber perturbation coefficient. When the reference beam quality Q_0 is ^{60}Co gamma radiation, k_{Q,Q_0} is simplified to k_Q . As this is the case throughout this work, from now on we will always refer to the beam quality correction factor as k_Q . For ^{60}Co , the product of $s_{w,air}$ and p is obtained as

a single factor, f_{Q_0} and is taken from the work of Andreo *et al.* [77]. For light ions, due to a lack of data, p_Q values are assumed to be unity with an associated standard uncertainty of 1%, and $(s_{w,air})_Q$ and $(W_{air})_Q$ are assumed to be identical for all light ion types. Together, these assumptions lead to an estimated relative standard uncertainty of 2.4% on the k_Q -factors presented in TRS-398 Rev. 1. A practical consequence is that beam quality specification is not yet implemented for light ion beams; TRS-398 Rev. 1 currently provides only a single set of chamber-specific k_Q values for light ions, making no distinction between carbon and helium ions.

In recent years, a few studies have addressed the determination of k_Q -factors in carbon ion beams. At the Heidelberg Ion-Beam Therapy Center (HIT, Heidelberg, Germany), Osinga-Blättermann *et al.* [154] and Holm *et al.* [98, 99] used water calorimetry to determine k_Q -factors for two types of cylindrical ionization chambers (PTW 30013 and IBA FC65-G) in the plateau region of scanned carbon ion beams and in the middle of a Spread-Out Bragg Peak (SOBP). Using these measurements, k_Q values for additional chamber types were determined using a cross-calibration approach [99, 155]. In addition to the experimental work, recent Monte Carlo studies have reported k_Q -factors for several chamber types [100–103, 156] (Houyoux *et al.* (submitted)). However, discrepancies up to 3% between experimental and Monte Carlo-based k_Q -factors have been observed, highlighting the need for further measurements and analysis. For helium ion beams, the first Monte Carlo-calculated k_Q -factors have recently been reported by Urago *et al.* [101] and Houyoux *et al.* (submitted), but, to the best of our knowledge, no experimental values have yet been published.

Therefore, in this work, water calorimetry was used to determine k_Q -factors in carbon and helium ion beams. Measurements were performed in the plateau region of several scanned single-layer carbon ion beams covering a range of clinically used energies (213.4 to 402.8 MeV/u), in order to assess any potential beam quality dependence. The measurements were performed at two therapy centers (HIT, where the prior experimental k_Q -factors in carbon ions were obtained [98, 99, 154, 155], and the MedAustron Ion Therapy Center (Wiener Neustadt, Austria)), under harmonized conditions to evaluate inter-center reproducibility of the results. In parallel, we report, for the first time, experimental k_Q values for helium ion beams, measured at both centers under similar conditions. Across all experiments, multiple cylindrical (IBA FC65-G and PTW 30013) and plane-parallel (IBA PPC05, IBA PPC40, PTW 34001, PTW 34045) ICs were included.

Collectively, these measurements (i) provide experimental k_Q -factors for

additional ionization chamber types in carbon ion beams, (ii) enable an assessment of potential beam quality dependence, (iii) test consistency across centers, (iv) deliver the first experimental k_Q -factors for helium ion beams, and (v) investigate chamber-to-chamber variability.

6.3 Materials and methods

6.3.1 Irradiation conditions

Carbon ion beams

Measurements in carbon ion beams were performed at both the MedAustron Ion Therapy Center and the Heidelberg Ion-Beam Therapy Center under similar conditions to enable an inter-center comparison. Both centers are synchrotron-based facilities providing different ion species [146, 157, 158]. All measurements were carried out in the plateau region at a water-equivalent depth of 4 cm. The TRS-398 Rev. 1 recommends depths of 1 cm or, alternatively, 2 cm, however these depths were not feasible with our calorimeter and vessel geometry. Within the plateau region, it is expected that the k_Q -factors show only minor variations with depth, based on the limited variation in stopping-power ratios [159] and Monte Carlo-calculated k_Q values (Houyoux *et al.* (submitted)). The field size was 10 cm $\times$ 10 cm for all conditions. At MedAustron, measurements were performed in single-layer scanned carbon ion beams with nominal energies of 213.4, 284.7, 346.6 and 402.8 MeV/u, corresponding to R_{80} values of 90, 150, 210 and 270 mm, respectively. Each field comprised 50 $\times$ 50 spots with 2 mm spot spacing. Beams were delivered with spill lengths of 1 s and spill pauses of 2.4 s and total field delivery took approximately 80 to 90 s depending on the energy. At HIT, measurements were performed in single-layer scanned carbon ion beams with nominal energies of 343.5 and 399.0 MeV/u, corresponding to R_{80} values of 209.9 and 269.3 mm, respectively. 51 $\times$ 51 spots were delivered with a spot spacing of 2 mm. The spill length was 4.5 s with beam-off time of 4 s and the total delivery of the field took approximately 135 and 150 s for the 343.5 and 399.0 MeV/u beams, respectively. Measurements at both centers were performed using ripple filters.

Helium ion beams

Measurements in helium ion beams were performed at both centers under similar conditions. At MedAustron, a nominal energy of 198.8 MeV/u was used and the field consisted of 50 $\times$ 50 spots with 2 mm spot spacing. The spill length was 1 s with pauses of 2.4 s, and the total field delivery was approximately 30 s.

At HIT, a nominal energy of 196.3 MeV/u was chosen and the field comprised 51 x 51 spots with 2 mm spot spacing. The spill length was 4.5 s with pauses of approximately 4 s, and the total delivery time was about 100 s. The corresponding R_{80} values were 250 mm at MedAustron and 249.4 mm at HIT. For both conditions, the measurement were performed in the plateau region at 4 cm depth. Similar to carbon ion beams, the k_Q -factors for helium ions are not expected to vary substantially with depth within this region [159] (Houyoux *et al.* (submitted)). The field size was again 10 cm × 10 cm and the ripple filters were inserted.

6.3.2 Water calorimetry

Principle

Water calorimetry is considered as the most direct method to determine absorbed dose to water by measuring the irradiation-induced temperature rise. The following equation is used to derive absorbed dose to water from water calorimetry measurements:

$$D_{w,Q}^{cal} = c_w \Delta T k_c k_p k_{HD} k_\rho k_{dd} \quad (6.2)$$

In this equation, c_w represents the specific heat capacity of water and ΔT the temperature rise measured during irradiation. A series of correction factors ($k_c, k_p, k_{HD}, k_\rho, k_{dd}$) are applied to account for non-ideal conditions, as discussed in detail in section 6.3.2.

Setup and operation of the water calorimeter

The water calorimeter used in this study was constructed based on the water calorimeter operated at McGill University (Montreal, Canada). Full technical details are available in the works of Renaud [106] and Sarfehnia [105], therefore, only a brief summary is provided here. The detector consists of a 30 cm × 30 cm × 30 cm water tank made out of PMMA, surrounded by expanded polystyrene for thermal insulation. The water inside is maintained at 4 °C by an internal heat exchanger connected to an external fridge to avoid convection. The water calorimeter is designed for horizontal beams and includes a 1 mm thick PMMA entrance window. A plane-parallel glass vessel is mounted inside the water tank. The position of the vessel is adjustable, allowing placement at different depths relative to the entrance window. Two thermistor probes are positioned within this vessel using a travelling microscope. Their tips face each other and are separated by 2 mm. Each probe contains a thermistor bead with

a nominal resistance of about 10 k Ω at 4 °C. For each irradiation, 60 s of pre- and post-drift intervals were measured. By linearly extrapolating these intervals to the mid-irradiation time, the irradiation induced signal was obtained. Measurements were acquired in sets of ten consecutive irradiations, followed by a one-hour break to allow the calorimeter to cool and re-stabilize before the next set.

Correction factors

As briefly mentioned in section 6.3.2, several correction factors were applied to the water calorimeter signal. The calorimeter was operated at a temperature of 4 °C to avoid convective heat transfer inside, however, conductive heat transfer still needs to be considered. Therefore, the heat transfer correction factor k_c was introduced, defined as the ratio of the temperature rise in ideal conditions (without conduction) and the actual temperature rise (with conduction). To determine k_c , finite-element simulations were performed using the COMSOL Multiphysics software (version 6.0). A 3D model of the water calorimeter was built incorporating the vessel and simplified thermistor geometry. The heat transfer equation was solved in time and space with material properties at 4 °C. The implemented heat source is based on the irradiation field, utilizing the percent depth dose (PDD) distributions. Given the scanned-beam delivery, the time-structure of the beam should be taken into account. Modeling every single spot individually would be too computationally demanding, and therefore an average spill-break sequence was used. The scanned field was divided into subsets corresponding to the spots delivered within a given spill, which were assumed to be delivered over the duration of a single spill, followed by a pause according to the irradiation pattern. In this way, the overall irradiation time structure was preserved while simplifying the detailed delivery sequence. The impact of this approximation was assessed by varying the assumed number of lines per spill and the spill and pause durations, resulting in only small differences in the calculated k_c values, which were included in the uncertainty budget. This approach was also used in the work of Holm *et al.* [160]. The same pre- and post-drift intervals as during the measurements were considered as well as the same number of consecutive runs. The final k_c values were then taken as the average over 10 consecutive irradiations.

The beam perturbation correction factor (k_p) is applied to correct for the perturbation of the beam that occurs due to the presence of the glass vessel. It is defined as the ratio of the dose at the thermistor position in an idealized all-water geometry (vessel and probe materials replaced by water) to the dose at the same point in the real geometry that includes the glass vessel and thermistor probes.

Monte Carlo simulations using GATE/Geant4 (v9.0, physics list QGSP BIC HP) were used to evaluate k_p . A full 3D model of the calorimeter was implemented, comprising the vessel and simplified representation of the thermistor probes. The dose was scored in a small volume coincident with the thermistor location. Two simulations were performed: (i) with all non-water materials replaced by water and (ii) with the true material composition. The value of k_p was then obtained as the ratio of the corresponding dose values at the measurement position.

The factor k_{HD} corrects for the heat defect, which is defined as the difference between the energy absorbed from the radiation and the energy that appears as heat. This effect arises from the radiolysis of water and impurities inside the vessel triggering chemical reactions. Detailed modeling and measurements have shown that ultrapure, hydrogen-saturated water that is pre-irradiated reaches a chemical steady state in which the net heat defect is zero. Under these conditions, a unity correction was assumed for k_{HD} , with an associated uncertainty of 0.14% [116, 132]. Importantly, although much of the foundational work was performed for low-LET radiation, Sassowsky & Pedroni [147] confirmed that this was also valid for higher LET radiation, and the same preparation has been used successfully in proton beams [143, 145, 148]. As there is no evidence of any LET dependence, the hydrogen-saturated pre-irradiated water system was also used in the carbon ion calorimetry studies performed at HIT [98, 99, 154], where a unity correction was adopted as well. As the vessel in our study was prepared using the same conditions, a correction of $k_{HD} = 1$ was applied for both carbon and helium ions. The preparation of the vessel was repeated before every measurement campaign.

While calorimetry measurements were conducted at 4 °C, the IC measurements were carried out at room temperature (approximately 20 °C to 22 °C). As the density of water differs slightly between these temperatures, there will be a small difference in measurement depth. To account for this, the water-density correction factor k_ρ was applied. By knowing the water density at the different temperatures, we can correct for this by using the PDDs of the different beams determined through Monte Carlo simulations (GATE/Geant4).

As the thermistor probes are not located on the central axis, there will be a slight difference in the dose measured at the thermistor location compared to the dose at the central axis. To account for this, correction factor k_{dd} is introduced. This correction factor is defined as the ratio of the dose on the central axis to the dose at the thermistor positions and is determined based on the lateral dose profiles obtained by means of either Monte Carlo simulations

(GATE/Geant4) or a Lynx detector (IBA Dosimetry).

6.3.3 IC measurements

Both plane-parallel and cylindrical ICs were evaluated. Four types of plane-parallel ICs were used (IBA PPC05 and PPC40, IBA Dosimetry (Schwarzenbruck, Germany); PTW 34001 (ROOS) and 34045 (Advanced Markus), PTW (Freiburg, Germany)) and two types of cylindrical ICs (IBA FC65-G and PTW 30013). For the IBA PPC05, IBA PPC40 and PTW 30013, two chambers of each type were included, for the other types only one chamber was measured. Not all chambers were included in every measurement campaign due to availability and time constraints. All IC measurements were performed under the same irradiation conditions as the calorimetry measurements, except the water was now at room temperature. The ICs were placed inside the water calorimeter phantom at 4 cm in dedicated holders and positioned according to TRS-398 Rev. 1 recommendations. For plane-parallel chambers, the reference point (the inner surface of the entrance window) was positioned at the measurement depth z_{ref} , considering the water-equivalent thickness of the entrance window. For the cylindrical chambers, the reference point (on the central axis) was positioned 0.75 times r_{cyl} deeper than z_{ref} , for both carbon and helium beams. The ionization chamber readings were corrected for temperature and pressure (k_{tp}), polarity (k_{pol}) and ion recombination (k_s) effects. Since water calorimetry provides a point measurement of absorbed dose to water, an additional volume correction was applied to account for the non-uniformity of the field over the ICs sensitive volume. An overview of the ICs used in this work, along with their operating voltage, absorbed dose to water calibration coefficient in ^{60}Co , $N_{D,w}$, and its corresponding uncertainty, are presented in table 6.1.

The chamber-specific $N_{D,w}$ -values of the IBA chambers were provided by the IBA Dosimetry Secondary Standard Dosimetry Laboratory (SSDL) (Schwarzenbruck, Germany), and are traceable to the Primary Standard of Absorbed Dose at the Physikalisch-Technische Bundesanstalt (PTB, Braunschweig, Germany). The PTW 30013 (#7887), PTW 34001 (#2460) and PTW 34045 (#1540) chambers were calibrated at the PTW Calibration Laboratory (Freiburg, Germany), also traceable to PTB. The PTW 30013 (#7776) was calibrated at Seibersdorf Laboratories (Austria), traceable to the Austrian Primary Standard of Absorbed Dose at the Bundesamt für Eich- und Vermessungswesen (BEV, Vienna, Austria).

IC	Voltage (V)	$N_{D,w}$ (Gy/C)	Uncertainty (%)
Plane-parallel			
IBA PPC05 #194	-300	6.178×10^8	0.5
IBA PPC05 #475	-300	5.846×10^8	0.5
IBA PPC40 #162	-300	9.533×10^7	0.5
IBA PPC40 #512	-300	8.172×10^7	0.5
PTW 34001 #2460	+200	8.396×10^8	0.75
PTW 34045 #1540	+300	1.329×10^9	0.55
Cylindrical			
IBA FC65-G #516	+300	4.817×10^7	1.1
PTW 30013 #7776	+400	5.335×10^7	0.7
PTW 30013 #7887	+400	5.376×10^7	0.55

Table 6.1: Overview of the ionization chambers used in this work, their operating voltage, absorbed dose to water calibration coefficients in ^{60}Co , and associated uncertainties ($k = 1$).

6.3.4 Determination of k_Q -factors

Following TRS-398 Rev. 1, the absorbed dose to water at beam quality Q obtained with an ionization chamber calibrated in terms of absorbed dose to water in a ^{60}Co reference beam is given by:

$$D_{w,Q}^{ion} = M_Q N_{D,w} k_Q, \quad (6.3)$$

where M_Q is the corrected chamber reading, $N_{D,w}$ the calibration coefficient obtained in the reference beam quality (^{60}Co), and k_Q the beam quality correction factor.

As dose to water obtained through calorimetry and ionometry should yield the same result, it can be stated that:

$$k_Q = \frac{D_{w,Q}^{cal}}{M_Q N_{D,w}}. \quad (6.4)$$

In this work, $D_{w,Q}^{cal}$ and M_Q were determined as described in sections 6.3.2 and 6.3.3, respectively. Substituting these values, together with the $N_{D,w}$ coefficients given in table 6.1, into the above equation yields the k_Q -factors obtained in this study.

6.4 Results

6.4.1 Water calorimetry

The correction factors applied to the calorimeter output were determined as described in section 6.3.2 and are presented in table 6.2 for the carbon ion beams and table 6.3 for the helium ion beams. Table 6.4 gives an overview of the total uncertainty budget for the determination of absorbed dose to water following the calorimetric measurement procedure as described above (section 6.3.2) in accordance with Lechner & Palmans [149].

Values for the heat conduction correction k_c ranged between 0.9996 and 1.0070 for the carbon ion beams and values of 0.9815 and 1.0053 were obtained for the helium ion beams. The observed variations in k_c are primarily attributed to differences in beam delivery time and to small variations in the positioning of the thermistor probes within the glass vessel between measurement campaigns. Shorter field delivery times result in steeper post-irradiation drift curves, reflecting ongoing heat transfer near the thermistor probes, which leads to larger corrections when applying the linear extrapolation procedure. In contrast, for longer delivery times, the heat deposited near the thermistor probes has more time to redistribute, resulting in flatter post-drift curves and smaller deviations from unity. In addition, the distance between the thermistor probes and the entrance window of the vessel influences the magnitude of the correction, with probes positioned closer to the entrance window leading to larger deviations from unity [161]. The correction has an estimated standard uncertainty of 0.40%, based on the combination of the type A uncertainty of the 10 consecutive runs and type B uncertainties considering material parameters, the input dose distribution and approximation of the time structure. Beam perturbation corrections k_p between 0.9972–0.9996 were applied based on the Monte Carlo simulations with an associated standard uncertainty of 0.15%. For the heat defect, no correction was assumed in all conditions as the vessel was filled with hydrogen-saturated ultrapure water and pre-irradiated before every measurement campaign. In the work of Holm *et al.* [98, 99], an uncertainty of 0.14% was attributed to this based on the work of Krauss [132] done in ^{60}Co radiation. In this work, a more conservative uncertainty of 0.30% is taken based on the work of Sassowsky & Pedroni [147], who investigated the heat defect for higher LET radiation. Since all measurements were performed in the plateau region, the corrections for the difference in water density (k_ρ) were minimal, ranging from 0.9996 to 1.000 for all conditions. The uncertainty for this correction is based on the uncertainty on the density of water [134]. The beam-profile non-uniformity correction factors (k_{dd}) were taken to be unity

with an associated uncertainty of approximately 0.25%. This uncertainty was estimated by evaluating k_{dd} for different thermistor positions varying ± 1 mm in every orthogonal direction.

Energy (MeV/u)	MedAustron				HIT	
	213.4	284.7	346.6	402.8	343.5	399.0
k_c	1.0008	1.0021	0.9997	0.9996	1.0069	1.0070
k_p	0.9972	0.9985	0.9993	0.9996	0.9992	0.9996
k_{HD}	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
k_ρ	0.9996	0.9999	1.0000	1.0000	1.0000	1.0000
k_{dd}	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000

Table 6.2: Correction factors applied to the water calorimeter output in carbon ion beams at MedAustron and HIT.

Energy (MeV/u)	MedAustron	HIT
	198.8	196.3
k_c	0.9815	1.0053
k_p	0.9986	0.9984
k_{HD}	1.0000	1.0000
k_ρ	0.9999	0.9999
k_{dd}	1.0000	1.0000

Table 6.3: Correction factors applied to the water calorimeter output in helium ion beams at MedAustron and HIT.

In addition to the uncertainties on the correction factors, contributions of the measured calorimeter signal, thermistor sensitivity, electronic calibrations, the specific heat capacity of water and positioning were included. For each beam condition, 20–30 calorimetric runs were performed, typically consisting of sets of ten consecutive irradiations. The repeatability of the calorimeter signal, expressed as the standard deviation of the mean, was on the order of 0.32–0.35%, and represents the only type A uncertainty. All other contributions are type B uncertainties. Since the uncertainties associated with the different beam energies showed only minor variations, the values listed in table 6.4 are considered applicable to all beam energies used in this study. Combining all

contributions gives a total standard uncertainty of 0.72% and 0.70% on $D_{w,Q}^{cal}$ for carbon ion and helium ions, respectively.

Quantity	Relative standard uncertainty (%)	
	Carbon ions	Helium ions
Calorimeter signal	0.35	0.32
Thermistor sensitivity	0.07	0.07
Electronic calibrations	0.20	0.20
Specific heat capacity c_w	0.05	0.05
Heat conduction k_c	0.40	0.40
Beam perturbation k_p	0.15	0.15
Heat defect k_{HD}	0.30	0.30
Density correction k_ρ	0.01	0.01
Beam profile k_{dd}	0.25	0.27
Positioning	0.10	0.05
$D_{w,Q}^{cal}$	0.72	0.70

Table 6.4: Uncertainty contributions ($k = 1$) to the calorimetric determination of absorbed dose to water ($D_{w,Q}^{cal}$) in carbon and helium ion beams.

6.4.2 IC measurements

Polarity corrections were assumed to be unity, with an associated relative standard uncertainty of 0.2%. Recombination corrections were generally small ($< 0.5\%$) for all chamber types in both carbon and helium ion beams, with the exception of the IBA FC65-G chamber used at MedAustron, for which corrections reached up to 1% in the carbon and helium ion beams. The recombination corrections were obtained using the two-voltage method given in TRS-398 Rev. 1 for continuous beams. This method might slightly underestimate the initial recombination and therefore an additional type B uncertainty was assigned to the correction factor. This contribution was estimated from measurements performed under similar beam conditions using a PPC40 ionization chamber, for which a Jaffé plot was acquired. The difference between the recombination correction factor k_s obtained from the full Jaffé plot analysis and that derived using the two-voltage method was found to be below 0.2%. The resulting ion recombination corrections obtained in this work are of the same order of magnitude as those reported in literature for similar carbon ion beam conditions

where full Jaffé plots were measured [99, 154, 155]. The full uncertainty budget on M_Q is presented in table 6.5. The volume correction was taken as unity, with an associated relative uncertainty of 0.26–0.30%, determined using the same method as the one applied to account for lateral dose-profile non-uniformity in the calorimetry measurements. Combining all components yields a total relative uncertainty of approximately 0.4% for the corrected chamber readings M_Q .

Quantity	Relative standard uncertainty (%)	
	Carbon ions	Helium ions
IC repeatability	< 0.10	< 0.10
Polarity correction	0.20	0.20
Ion recombination correction	0.17	0.17
Temperature–pressure correction	0.08	0.08
Volume correction	0.26	0.30
Electrometer correction	0.10	0.10
Positioning	0.10	0.05
M_Q	0.42	0.43

Table 6.5: Uncertainty budget ($k = 1$) for the corrected IC readings (M_Q) in carbon and helium ion beams.

6.4.3 Determination of k_Q -factors

The k_Q -factors were obtained according to equation 6.4 and are presented in table 6.6 for the carbon ion beams and table 6.7 for the helium ion beams. The total standard uncertainty on the k_Q -factors was obtained by combining the contributions from $D_{w,Q}^{cal}$ (table 6.4), M_Q (table 6.5), and $N_{D,w}$ (table 6.1) assuming statistical independence. This resulted in total standard uncertainties ranging from 0.96% to 1.38% across all investigated conditions.

IC / Energy (MeV/u)	MedAustron			HIT		
	213.4	284.7	346.6	402.8	343.5	399.0
Plane-parallel						
IBA PPC05 #194	–	–	–	–	0.9866(97)	0.9853(97)
IBA PPC05 #475	0.9974(97)	1.0066(98)	1.0066(98)	1.0046(97)	0.9981(97)	0.9981(97)
IBA PPC40 #162	–	–	0.9837(95)	–	0.9766(95)	0.9794(95)
IBA PPC40 #512	–	0.9773(95)	0.9842(96)	0.9801(95)	0.9734(94)	0.9764(95)
PTW 34001 #2460	–	–	0.9964(112)	–	0.9866(110)	0.9904(111)
PTW 34045 #1540	–	–	0.9983(100)	–	0.9985(100)	0.9890(99)
Cylindrical						
IBA FC65-G #516	–	–	1.0254(142)	–	1.0070(138)	1.0114(138)
PTW 30013 #7776	–	–	1.0247(112)	–	1.0183(111)	1.0200(111)
PTW 30013 #7887	–	–	1.0256(103)	–	1.0161(102)	1.0202(102)

Table 6.6: k_Q -factors obtained in carbon ion beams at MedAustron and HIT. Numbers in parentheses represent the standard uncertainty ($k = 1$) in the last two or three digits.

	MedAustron	HIT
Energy (MeV/u)	198.8	196.3
Plane-parallel		
IBA PPC05 #194	1.0019(96)	0.9906(95)
IBA PPC05 #475	1.0118(97)	1.0014(96)
IBA PPC40 #162	0.9859(95)	0.9768(94)
IBA PPC40 #512	0.9851(95)	0.9760(94)
PTW 34001 #2460	1.0007(111)	0.9881(110)
PTW 34045 #1540	1.0054(101)	1.0050(101)
Cylindrical		
IBA FC65-G #516	1.0185(140)	1.0036(138)
PTW 30013 #7776	1.0223(110)	1.0165(110)
PTW 30013 #7887	–	1.0210(102)

Table 6.7: k_Q -factors obtained in helium ion beams at MedAustron and HIT. The numbers in parentheses represent the standard uncertainty ($k = 1$) on the last two or three digits.

Table 6.8 presents chamber-type mean k_Q values for each particle type, derived from all individual measurements. Uncertainty propagation for the averaged values accounted for both correlated and uncorrelated components, with partially correlated corrections treated as 50% correlated. For most chamber types, the agreement between different units of the same chamber type was good, and the mean k_Q value was therefore calculated as the average of the individual data points. For the IBA PPC05 chamber, however, a larger chamber-to-chamber variability was observed and the number of measurements differed between individual chambers. Therefore, chamber-specific weighted averaging was applied, and an additional chamber-variability component was included in the total uncertainty.

6.5 Discussion

This study provides a comprehensive set of experimentally determined beam quality correction factors for carbon and helium ion beams based on water calorimetry measurements performed under harmonized conditions at two independent particle therapy centers. The results allow an assessment of beam

quality dependence, inter-center reproducibility, and enable a direct comparison with existing experimental data, Monte Carlo simulations, and the recommendations of TRS-398 Rev. 1.

IC	Carbon ions		Helium ions	
	k_Q	n	k_Q	n
Plane-parallel				
IBA PPC05	0.994(11)	8	1.001(11)	4
IBA PPC40	0.979(7)	8	0.981(8)	4
PTW 34001	0.991(10)	3	0.994(10)	2
PTW 34045	0.995(8)	3	1.005(9)	2
Cylindrical				
IBA FC65-G	1.015(13)	3	1.011(13)	2
PTW 30013	1.021(7)	6	1.020(8)	3

Table 6.8: Mean k_Q -factors for each IC type in carbon and helium ion beams. The numbers in parentheses represent the standard uncertainty ($k = 1$) on the last one or two digits and n indicates the number of individual data points.

6.5.1 Carbon ions

Beam quality dependence

Figure 6.1 shows all the individual data points obtained in this work for carbon ions. Across the investigated carbon ion energies (213.4 to 402.8 MeV/u), no systematic dependence of k_Q on nominal beam energy was observed for any of the investigated ionization chamber types. Variations between individual measurements were comparable to the experimental uncertainty and showed no consistent trend. It should be noted that the reported uncertainties include both correlated and uncorrelated components and therefore, the apparent agreement between individual data points within a given chamber type may be influenced by shared uncertainty contributions. Similar conclusions were reported by Holm *et al.* for the chambers used in their work [99]. Consequently, chamber-type mean k_Q values were derived and are considered representative for plateau measurements under the investigated conditions.

Inter-center comparison

Beam quality correction factors were measured under harmonized experimental conditions at MedAustron and HIT to allow a direct inter-center comparison. At MedAustron, nominal carbon ion beam energies of 346.6 and 402.8 MeV/u were used, while at HIT energies of 343.5 and 399.0 MeV/u were selected, with corresponding R_{80} values differing by less than 1 mm between both centers. For all investigated chamber types, the k_Q -factors obtained at MedAustron and HIT agree within the combined standard uncertainties, demonstrating good reproducibility of the measurements across facilities. A systematic offset is nevertheless observed, with k_Q values measured at MedAustron generally being larger than those obtained at HIT, with the exception of the PTW 34045 chamber. The largest difference is observed for the IBA FC65-G chamber, amounting to approximately 1.7%. However, this difference remains within the combined uncertainties.

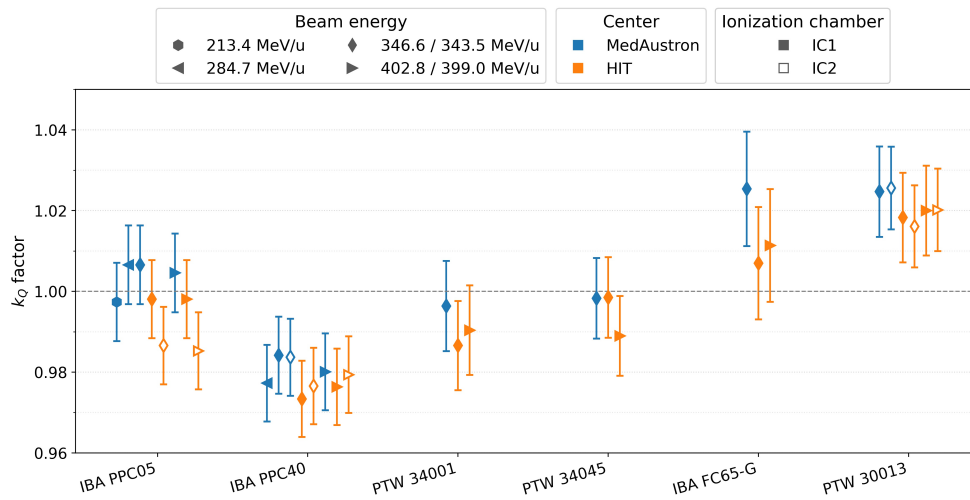


Figure 6.1: Individual k_Q -factors obtained in this work in carbon ion beams for all investigated ionization chamber types. Different marker shapes correspond to different beam energies; measurements performed at MedAustron and HIT at similar nominal beam energies (346.6/343.5 MeV/u and 402.8/399.0 MeV/u) are represented using the same marker shape. For each chamber type, data points are arranged in order of increasing beam energy from left to right. Results obtained at MedAustron are shown in blue, while those obtained at HIT are shown in orange. White-filled markers indicate measurements performed with a second ionization chamber of the same type. Error bars indicate standard uncertainties ($k = 1$).

The observed differences may be related to subtle difference between the beamlines at MedAustron and HIT. In particular, differences in the temporal beam structure and total irradiation time can influence the heat conduction, as discussed previously. In addition, variations in lateral beam uniformity and scanning patterns may affect the local dose distribution at the measurement position. Differences in beam monitoring systems and beam-shaping devices, such as ripple filters, may also introduce small systematic effects. Furthermore, uncertainties related to detector positioning and recombination may contribute to the observed variations. While these effects are expected to be small and within the reported uncertainties, they may contribute to the systematic differences observed between the two facilities.

Comparison with literature data

The chamber-type mean k_Q values derived in this work for carbon ion beams are compared with previously published experimental data, Monte Carlo-based data and TRS-398 Rev. 1 recommendations in figure 6.2. The experimental comparison includes direct water calorimetry measurements performed in the plateau region of monoenergetic carbon ion beams for the IBA FC65-G and PTW 30013 chambers. These measurements were originally reported by Osinga-Blättermann *et al.* [154] for a 429 MeV/u beam and later revised by Holm *et al.*, who extended the dataset with additional measurements at 287 MeV/u [99]. As no beam quality dependence was observed, the average for these two beam energies is shown. Based on the same 429 MeV/u dataset, cross-calibrated k_Q values for the IBA PPC05, IBA PPC40 and PTW 34001 chambers reported by Osinga-Blättermann & Krauss [155] and subsequently corrected by Holm *et al.* [99] are also included. The values recommended in TRS-398 Rev. 1 were taken as the average of the calculated value (equation 6.1) and the experimental value, for those chamber types for which experimental data were available.

For all chamber types except the IBA PPC05, excellent agreement is observed between the experimentally determined k_Q values. The mean values obtained in this work agree within approximately 0.5% with both the direct calorimetric measurements for the IBA FC65-G and PTW 30013 chambers and the cross-calibrated values for the IBA PPC40 and PTW 34001 chambers. The associated experimental uncertainties are of similar magnitude across the different studies, ranging from 0.7% to 1.3%, further supporting the consistency of the experimental dataset.

Monte Carlo-derived k_Q values have been reported by several independent groups. Stolzenberg *et al.* [102] performed simulations under beam conditions

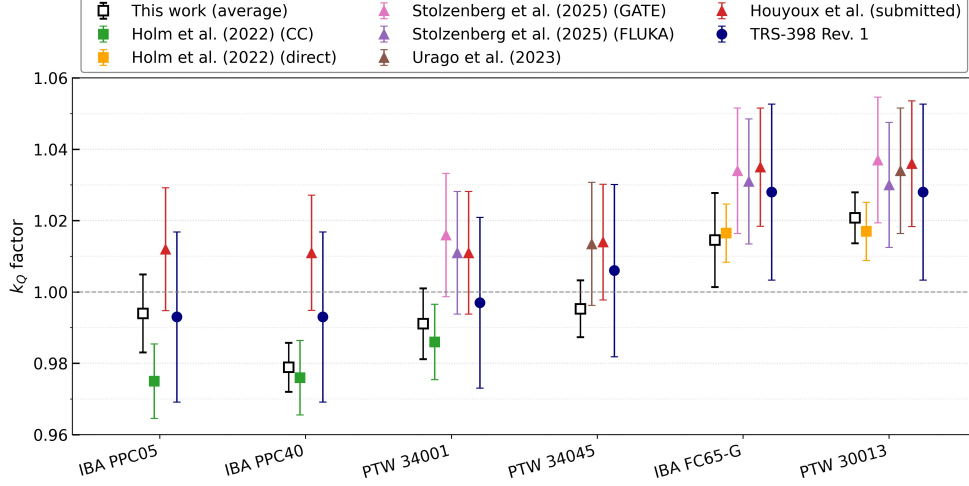


Figure 6.2: Comparison of the k_Q -factors in carbon ion beams obtained in this work with published experimental data, Monte Carlo-derived values and the TRS-398 Rev. 1 [6] recommendations. The average value obtained in this work is shown for each chamber type. The experimental results reported by Holm *et al.* [99] were derived either from direct water calorimetry measurements or through cross-calibration (CC). All experimental data are indicated by squares. Monte Carlo-based results reported by Stolzenberg *et al.* [102], Urago *et al.* [100] and Houyoux *et al.* (submitted) are shown as triangles. TRS-398 Rev. 1 recommendations are indicated by circles. Error bars represent standard uncertainties ($k = 1$).

matching the experimental measurements of Holm *et al.* [99] using two different codes (GATE/Geant4 and FLUKA). For completeness, results from both codes are shown. Urago *et al.* reported Monte Carlo-based k_Q -factors in carbon ion beams for the PTW 34045 and PTW 30013 chambers [100]. In addition, Houyoux *et al.* (submitted) reported Monte Carlo values averaged over multiple beam energies for all chamber types investigated in the present work.

Very good agreement is observed among the Monte Carlo results obtained by the different groups, with reported standard uncertainties of the order of 1.6–1.7%. Nevertheless, a systematic difference is apparent between Monte Carlo-derived and experimentally determined k_Q -factors. For the cylindrical chambers, Monte Carlo values are consistently larger than the experimental values by approximately 1-2%, while for the plane-parallel chambers the differences reach up to about 3%. This systematic behavior is observed for all chamber types and across different Monte Carlo codes.

The standard uncertainty reported for the k_Q -factors obtained through Monte Carlo simulations is dominated by the uncertainty on the W_{air} -value, which is 1.5% [75]. This constitutes the main limitation on the achievable accuracy of Monte Carlo-derived k_Q -factors and may partly explain the systematic offset observed between experimental and simulation-based results. Further investigation is required to fully understand and resolve these differences.

For the IBA PPC05 chamber, the observed behavior requires particular consideration. In the present work, measurements performed with two IBA PPC05 chambers under identical conditions revealed a reproducible chamber-to-chamber variability of approximately 1.3%. When comparing experimental data with Monte Carlo-derived k_Q -factors, differences ranging from about 1% to 3% are observed. A deviation of approximately 1% is found for the IBA PPC05 #475 chamber used in this study, whereas a difference up to 3% is observed for the value reported by Holm *et al.* obtained through cross-calibration [99]. Notably, in that work a polarity correction of approximately 1.6% was reported for their PPC05 chamber in the ^{60}Co reference beam [155], which is considerably larger than values typically reported for plane-parallel chambers [82, 162]. Despite this large correction, the measurements were nevertheless included in their analysis. In addition, larger deviations of k_Q values for this chamber type have also been observed in proton beams [133]. These findings suggest that chamber-to-chamber variability for the IBA PPC05 may be substantially larger than for other chamber types and should therefore be carefully considered when interpreting and comparing k_Q values. As the PPC05 is a relatively small-volume chamber compared to Roos-type and Farmer-type chambers, small manufacturing differences may have a comparatively larger impact on the chamber response. In contrast, good agreement was observed between the two units of the PTW 30013 and IBA PPC40 chamber types.

6.5.2 Helium ions

The k_Q -factors obtained in helium ion beams in this work are shown in figure 6.3 and compared across the two different centers, MedAustron and HIT. The results are further compared with Monte Carlo-derived values reported by Urago *et al.* [101] and Houyoux *et al.* (submitted), as well as with the values recommended for light ions in TRS-398 Rev. 1. All individual data points as well as the average value per chamber type are shown. For all investigated chamber types, a systematic trend is observed whereby the k_Q -factors measured at MedAustron are higher than those measured at HIT. Nevertheless, for all chambers, the results obtained at the two centers agree within the combined

standard uncertainties. The smallest inter-facility difference is observed for the PTW 34045, for which almost identical values are obtained, while the largest difference, approximately 1.5%, is found for the IBA FC65-G chamber.

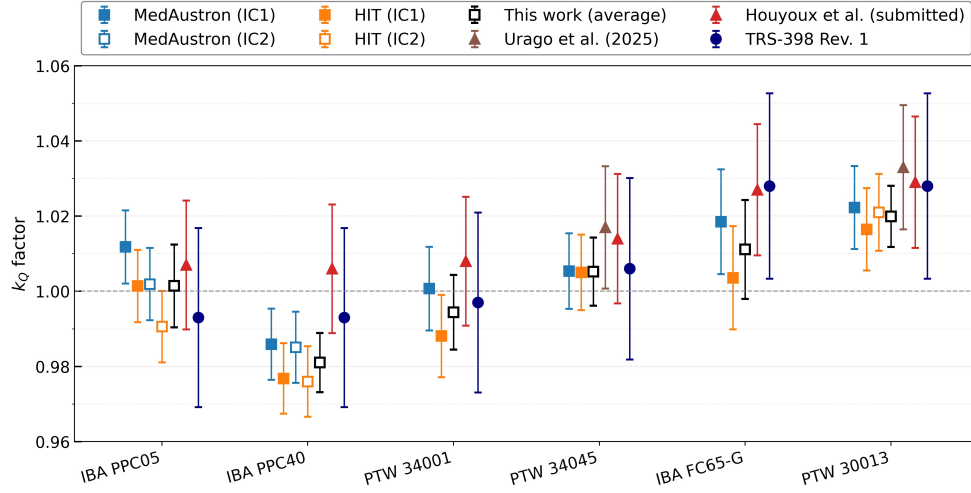


Figure 6.3: Comparison of k_Q -factors in helium ion beams obtained in this work with Monte Carlo data reported in literature and TRS-398 Rev. 1 recommendations. Experimental results from this study are shown as squares and include measurements performed at MedAustron (198.8 MeV/u) and HIT (196.3 MeV/u) using two ionization chambers of the same type (IC1 and IC2), as well as the corresponding mean value for each chamber type. Monte Carlo results reported by Urago *et al.* (150 MeV/u) [101] and Houyoux *et al.* (submitted) (175 MeV/u) are shown as triangles. TRS-398 Rev. 1 recommendations are indicated by circles. Error bars indicate standard uncertainties ($k = 1$).

Comparison with the Monte Carlo data of Urago *et al.* [101] and Houyoux *et al.* (submitted), reported with standard uncertainties of 1.6-1.7%, shows agreement within the combined uncertainties for all chamber types. In line with the findings for carbon ion beams, an offset is observed, with the Monte Carlo-derived k_Q -factors being consistently larger than the experimentally determined values. The largest deviation is observed for the IBA PPC40 chamber, amounting to approximately 2.5%, while differences for the other chamber types remain below 1.5%. Overall, the magnitude of the difference between the experimental and Monte Carlo data is slightly smaller than that observed in carbon ion beams. The consistency of this offset across different chamber types and Monte Carlo codes suggests again a systematic origin, potentially related to the adopted W_{air} value.

For the IBA PPC05 chambers, a difference of approximately 1% was observed between the two chambers of the same type measured under identical conditions, again consistent with the behavior seen in carbon ion beams. This suggests the presence of a small chamber-to-chamber variability for this ionization chamber type across particle types. In contrast, good agreement was observed between chambers of the same type for the IBA PPC40 and PTW 30013.

6.6 Conclusion

This work presents a comprehensive set of experimentally determined beam quality correction factors for light ion beams, including new data for carbon ions across multiple ionization chamber types and the first experimental k_Q -factors for helium ion beams. Using water calorimetry to perform measurements under harmonized conditions at two independent particle therapy centers enabled a robust assessment of beam quality dependence, inter-center reproducibility, and chamber-specific behavior.

For carbon ion beams, no notable dependence of k_Q on nominal beam energy was observed over the investigated range. Measurements performed at MedAustron and HIT showed agreement within combined standard uncertainties for all investigated chamber types, demonstrating good reproducibility across facilities. Chamber-to-chamber variation was generally small, supporting the use of chamber-type mean values, with the exception of the IBA PPC05 chamber, for which inter-chamber variability reached up to 1.3%. Comparison with previously published experimental data confirms good agreement with water calorimetry-based measurements and cross-calibrated values. In contrast, a systematic offset persists between experimentally determined and Monte Carlo-derived k_Q -factors, with simulation results consistently higher by approximately 1-3%, depending on chamber type. This behavior is observed across multiple Monte Carlo codes and independent studies, suggesting that this systematic offset may be related to common input quantities used in all simulations, such as W_{air} and/or $s_{w,air}$.

The helium ion measurements reported here constitute the first experimental dataset for this particle type. Overall, the obtained k_Q -factors show similar trends as those observed for carbon ions, including inter-center agreement and a consistent offset with respect to Monte Carlo-derived values.

Overall, this work substantially strengthens the experimental database of k_Q -factors for light ion beams, providing essential input for future refinements of the

TRS-398 Rev. 1 Code of Practice and highlighting the continued importance of calorimetry-based measurements in resolving remaining discrepancies between experimental and simulation based k_Q -factors.

Chapter 7

Water and graphite calorimetry comparison in carbon ion beams

The content presented in this chapter is based on a manuscript in preparation, and includes some preliminary data. The graphite calorimeter measurements and analysis were carried out by collaborators at the National Physical Laboratory (NPL).

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7.1 Summary

Objective: To perform a direct comparison between a water and graphite calorimeter in terms of absorbed dose to water in carbon ion beams.

Approach: Measurements were carried out in single-layer scanned carbon ion beams with nominal energies of 213.4, 284.7, and 402.8 MeV/u at the MedAustron Ion Therapy Center. Absorbed dose to water was determined using the UCLouvain water calorimeter and the NPL graphite calorimeter under identical irradiation conditions in the plateau region at 4 cm water-equivalent depth. In addition, measurements were performed with four plane-parallel ionization chamber types (PTW 34001, PTW 34045, IBA PPC05, and IBA PPC40), including multiple units per type, to compare with the calorimetric results.

Main results: The absorbed dose to water values obtained with the water and graphite calorimeters differed by 1.2%, 1.5%, and 1.2% for the investigated beam energies. As some correction factors for the graphite calorimeter are still under evaluation, these results should be considered preliminary, and the agreement is expected to improve slightly once these corrections are finalized. Ionization chamber measurements showed good reproducibility between campaigns and low chamber-to-chamber variability (within 0.4%). Slightly larger deviations between ionization chamber measurements and calorimetry were observed at the lowest beam energy, potentially influenced by positioning sensitivity and/or beam quality effects.

Significance: This work provides the first direct comparison between water and graphite calorimetry in carbon ion beams under identical conditions. The preliminary results indicate agreement between the two calorimeters, supporting the consistency of these independent calorimetric techniques.

7.2 Introduction

Reference dosimetry in carbon ion therapy is currently associated with substantially larger uncertainties than in photon or proton therapy. According to the IAEA Code of Practice TRS-398 Rev. 1, the relative standard uncertainty on the determination of absorbed dose to water under reference conditions is approximately 2.6–2.7% in carbon ion beams, compared to about 1% in high-energy photon beams and 1.7% in proton beams [6]. This difference is largely driven by the uncertainty associated with the beam quality correction factors, k_Q , which account for the difference in beam quality between the user beam and the reference beam used for the calibration of ionization chambers. Because very limited experimental data is currently available for k_Q -factors in carbon ion beams, the values recommended in TRS-398 Rev. 1 are based primarily on theoretical calculations and have an associated uncertainty of approximately 2.4%. In addition, several studies have reported discrepancies between experimentally determined and Monte Carlo-calculated k_Q values in carbon ion beams. As the overall uncertainty on the delivered dose is recommended to remain below 5%, the uncertainty associated with the determination of absorbed dose under reference conditions should ideally be around 1%, which is currently far from achieved in carbon ion therapy [4, 5, 163].

Calorimetry provides the most direct method for determining absorbed dose, as it measures the irradiation-induced temperature rise in a medium. Two calorimetric approaches have predominantly been developed for radiotherapy dosimetry: water calorimetry and graphite calorimetry, each with specific advantages and limitations. Water calorimeters measure the quantity of interest, absorbed dose to water, directly, and therefore provide the most direct realization of this quantity. However, the relatively high heat capacity of water reduces the sensitivity of the detector. In addition, chemical reactions in the water can influence the measured temperature rise, a phenomenon known as the heat defect, and therefore the purity and chemical state of the water must be carefully controlled [115–117]. Graphite calorimeters, in contrast, have a specific heat capacity that is approximately six times lower than that of water, making them inherently more sensitive. Their main limitation is that they measure absorbed dose to graphite, which must be converted to absorbed dose to water using a conversion factor. This conversion is the largest contribution to the overall uncertainty on the absorbed dose to water determined using graphite calorimeters [58].

Both calorimetric techniques have been successfully applied in proton beams [94, 95, 97, 106, 133, 143, 148, 164, 165]. In particular, the National Physical

Laboratory (NPL, Teddington, UK) has developed a portable graphite calorimeter capable of primary-standard level absorbed dose measurements in clinical proton beams, with an associated standard uncertainty of approximately 0.9% [166–168]. These developments represent a major step toward reducing uncertainties in proton therapy reference dosimetry. In carbon ion beams, both water and graphite calorimeters have also been applied independently [98, 99, 154, 169, 170]. However, experimental calorimetric data remains substantially more limited than for photons or protons. Furthermore, no direct comparison between the two independent approaches has previously been performed under identical beam conditions.

In this work, a direct comparison between the NPL graphite calorimeter (Gcal) and the UCLouvain water calorimeter (Wcal) is performed in the plateau region of single-layer scanned carbon ion beams with nominal beam energies of 213.4, 284.7, and 402.8 MeV/u. In addition, four ionization chamber types (PTW 34001, PTW 34045, IBA PPC05, and IBA PPC40), with multiple units of each type, are included in the comparison. This study therefore provides a unique cross-comparison between two independent calorimeter techniques and enables an important verification of absorbed dose to water determinations in carbon ion beams.

7.3 Materials and methods

7.3.1 Irradiation conditions

Measurements were performed in the research room at the MedAustron Ion Therapy Center (figure 7.1) using single-layer scanned carbon ion beams [146]. The beams were generated by a synchrotron and had nominal energies of 213.4, 284.7, and 402.8 MeV/u, corresponding to R_{80} values of 90, 150, and 270 mm, respectively. The beams were delivered in spills of 1 s duration with inter-spill pauses of approximately 2.4 s. The total field delivery time for a single field was approximately 80-90 s for all beam energies. The fields had a size of 10 cm $\times$ 10 cm and were delivered using a grid of 50 $\times$ 50 spots with a spot spacing of 2 mm. Measurements were performed in the plateau region at a water-equivalent depth of 4 cm. Ripple filters were inserted for all measurements.

7.3.2 Water calorimetry

The design and operation of the water calorimeter used in this study were described in detail in chapter 3, and a brief overview was also provided in the

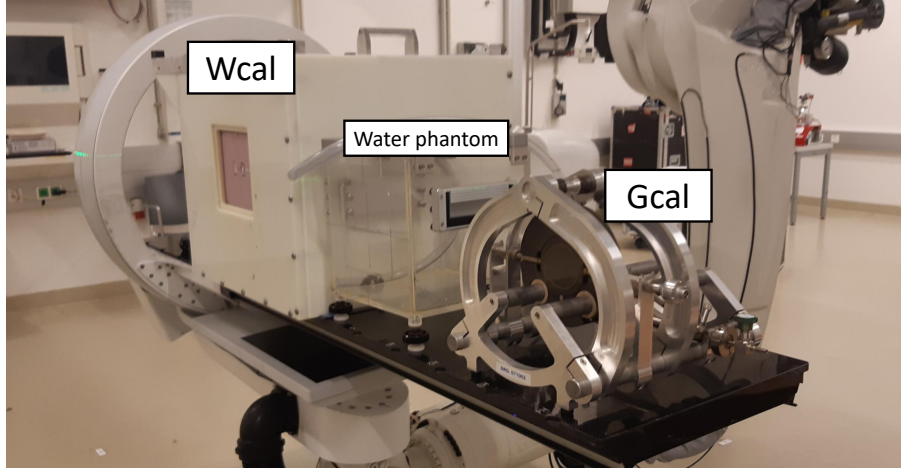


Figure 7.1: Picture of the water calorimeter (Wcal), the water phantom, and the graphite calorimeter (Gcal) on the treatment couch in the research room at MedAustron.

other experimental chapters (4-6). As the calorimeter setup and operating conditions were identical for the present measurements, the full description is not repeated here.

The correction factors applied to determine absorbed dose to water in carbon ion beams were already introduced in chapter 6. In particular, the same correction factors were used for the conductive heat transfer (k_c), the heat defect (k_{HD}), the water density (k_ρ), and the correction for the non-uniformity of the lateral dose profile (k_{dd}). The only difference between the present work and the measurements described in chapter 6 concerns the perturbation correction factor k_p .

When determining the k_Q -factors as presented in chapter 6, both the water calorimeter and ionization chamber measurements were performed inside the water calorimeter phantom. Consequently, the perturbation correction factor only accounted for the presence of the glass vessel and thermistor probes, since the perturbations from the remaining calorimeter components were identical for both measurement conditions. In the present study, the absorbed dose to water determined with the water calorimeter is compared to measurements using the graphite calorimeter and ionization chambers positioned in a water phantom.

Therefore, the perturbation caused by the entire calorimeter phantom must be considered. This was evaluated using two separate Monte Carlo simulations performed with GATE/Geant 4 (v9.0). The first simulation, as described in chapter 6, accounts for the perturbation of the glass vessel and thermistor probes, while the second simulation evaluates the perturbation introduced by the calorimeter phantom. The resulting contributions are multiplied to obtain the final k_p value for the considered beam conditions. To experimentally verify this correction, additional measurements were performed with an ionization chamber positioned inside the water calorimeter and subsequently in the water phantom, allowing for a direct comparison between the two geometries.

7.3.3 Graphite calorimetry

Setup and operation

The graphite calorimeter used in this work is the UK Primary Standard proton calorimeter developed at NPL. A detailed description of the system can be found in the work of Lourenço *et al.* [166, 167, 171] as well as in the IPEM Code of Practice for proton dosimetry by Green *et al.* [168].

A picture of the graphite calorimeter and its main components is shown in figure 7.2. The calorimeter consists of a graphite core surrounded by concentric graphite jackets, all enclosed within a graphite mantle. The components are disc-shaped, with the core having a diameter of 16 mm and a thickness of 2 mm (matching the sensitive volume of the PTW 34001 Roos and IBA PPC40 chambers). The different layers are separated by high-quality vacuum gaps in order to minimize heat transfer between the components. Both sensing and heating thermistors are embedded in the different graphite elements, allowing each component to be thermally controlled independently. This enables operation of the calorimeter in two different modes: quasi-adiabatic and isothermal mode [68].

In quasi-adiabatic mode, the absorbed energy in the graphite core is determined from the irradiation-induced temperature rise, which is proportional to the specific heat capacity of graphite. In isothermal mode, the calorimeter is maintained at a constant temperature using electrical heating, and the absorbed dose is derived from the reduction in electrical power required to maintain thermal equilibrium during irradiation. Measurements in this work were performed in both modes for all investigated beam energies. In both modes, the absorbed dose to water is obtained from:

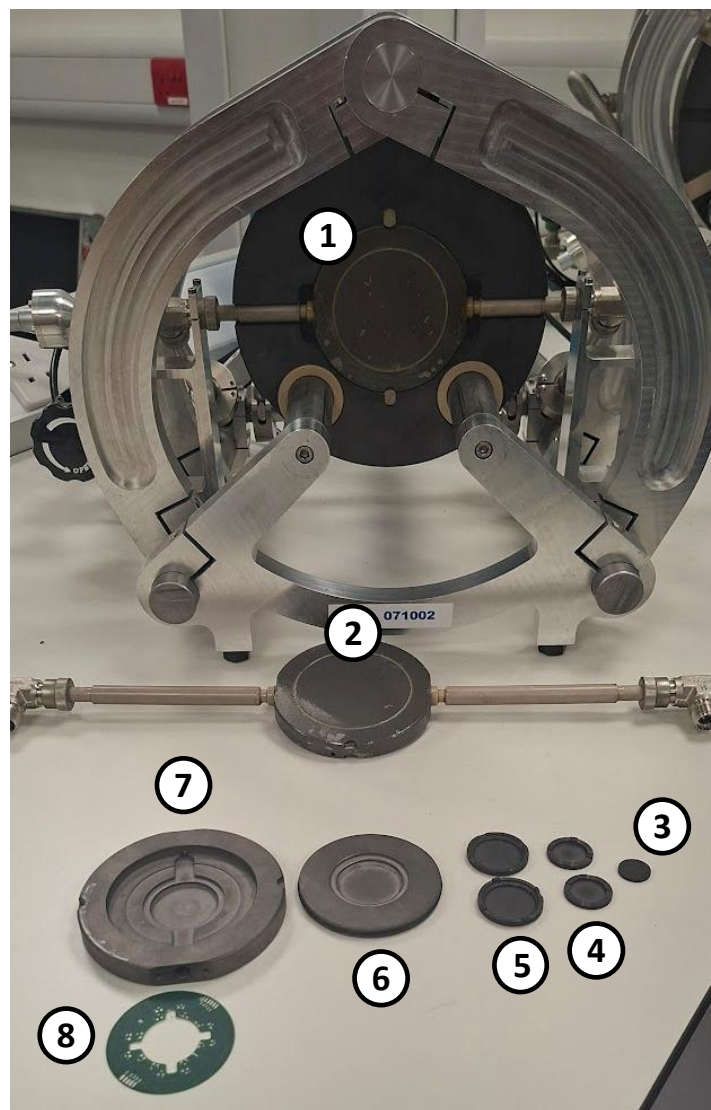


Figure 7.2: The NPL graphite calorimeter and its main components: (1) the graphite calorimeter, (2) inner assembly component and vacuum pipes, (3) graphite core, (4) inner jacket (front/back), (5) outer jacket (front/back), (6) mantle lid, (7) mantle base, (8) printed circuit board. Adapted from [166].

$$D_{w,Q}^{Gcal} = \frac{E_{core}^{rad}}{m_{core}} \cdot k_{imp} \cdot k_{gap} \cdot s_{w,g} \cdot k_{fl} \cdot k_{z,cal} \quad (7.1)$$

where E_{core}^{rad} is the energy imparted to the graphite core by the radiation and m_{core} is the mass of the graphite core, followed by a series of correction factors described below.

In quasi-adiabatic mode, E_{core}^{rad} is determined as the product of the core mass m_{core} , the specific heat capacity of graphite c_p , and the temperature rise, ΔT , measured by the sensing thermistors. In isothermal mode, the absorbed energy is obtained from the reduction in electrical heating power required to maintain a constant temperature and is calculated as the negative time integral of the change in electrical power supplied to the core.

Correction factors

The determination of absorbed dose to water using graphite calorimetry required the application of several correction factors. The impurity correction factor, k_{imp} , accounts for the presence of non-graphite materials within the core, such as thermistors, epoxy, and electrical wiring. It is defined as the ratio of the average dose to the graphite core in an ideal homogeneous graphite geometry to that in the actual geometry including these materials. k_{gap} accounts for the presence of the vacuum gaps between the different graphite layers. It is defined as the ratio of the dose to the core in a homogeneous graphite geometry (with the same amount of graphite but without the gaps) to that in the real geometry including the vacuum gaps. Both k_{imp} and k_{gap} are typically determined using Monte Carlo simulations [172]. The conversion from absorbed dose to graphite to absorbed dose to water is performed using the product $s_{w,g}k_{fl}$, where $s_{w,g}$ is the water-to-graphite mass stopping power ratio and k_{fl} is the fluence correction factor [173, 174]. This conversion is obtained through Monte Carlo simulations using FLUKA (version 2025.1.2). $k_{z,cal}$ accounts for deviations from the reference point of measurement. Since the measurements are performed at the same reference point as in the water calorimeter, this correction factor is taken as unity with an associated uncertainty.

7.3.4 Ionometry

The following plane-parallel ionization chamber types were included in the measurements: PTW 34001 (Roos), PTW 34045 (Advanced Markus), IBA PPC05, and IBA PPC40. Three Roos chambers (#2460, #2898, #2899), two Advanced Markus (#2343 and #2345), three PPC05 (#475, #1630, #1632), and two

PPC40 chambers (#508 and #512) were used. The ionization chamber measurements were performed in a PTW 34023 water phantom. The chambers were positioned at a water-equivalent depth of 4 cm, corresponding to the measurement depth used for the calorimeter measurements, while taking into account the water-equivalent thickness of the entrance window. The determination of absorbed dose to water with the ionization chambers was performed according to the $N_{D,w}$ -formalism described in TRS-398 Rev. 1:

$$D_{w,Q}^{ion} = N_{D,w,Q_0} M_Q k_Q \quad (7.2)$$

where N_{D,w,Q_0} is the chamber calibration coefficient in the reference beam quality Q_0 , M_Q is the corrected chamber reading, and k_Q is the beam quality correction factor.

All ionization chambers and electrometers used in this work were calibrated at the National Physical Laboratory (NPL). Calibration coefficients (N_{D,w,Q_0}) were obtained in a ^{60}Co reference beam, with associated standard uncertainties of 0.65% ($k = 1$). The chamber readings were corrected for temperature and pressure (k_{tp}) and ion recombination (k_s). Ion recombination was evaluated using the two-voltage method described in TRS-398 Rev. 1 for continuous beams. As this method may slightly underestimate the recombination under the present beam conditions, an additional uncertainty component was included to account for this effect. The polarity correction (k_{pol}) was not measured in the carbon ion beams and was therefore assumed to be unity, with an additional uncertainty included to account for this assumption. The k_Q -factors were taken from TRS-398 Rev. 1 [6].

7.3.5 Detector positioning

While the calorimetry measurements were performed during a single measurement campaign (campaign 2), the ionization chamber measurements were carried out over three campaigns: before the calorimetry measurements (campaign 1), during the calorimetry measurements (campaign 2), and after the calorimetry measurements (campaign 3). During the first campaign, the ionization chambers were positioned in the water phantom at a water-equivalent depth of 4 cm, with the entrance window of the water phantom aligned at isocenter (position 1). For the calorimetry measurements, however, the front surface of the water calorimeter was aligned with isocenter. Although the measurements were also performed at a water-equivalent depth of 4 cm, the presence of expanded polystyrene in front of the sensitive volume resulted in a

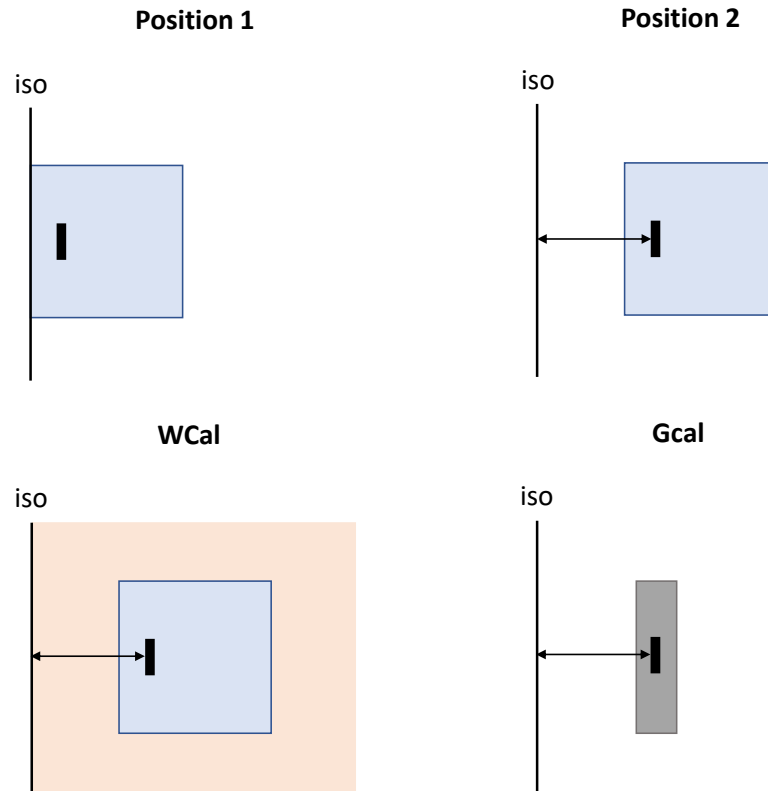


Figure 7.3: Schematic overview of the detector positions used during the measurements. In position 1, the water phantom entrance was aligned with the isocenter. In position 2, the positioning mimicked the water calorimeter setup, resulting in a physical distance of 13.81 cm between the isocenter and the effective point of measurement (indicated by the arrow). The graphite calorimeter was positioned to achieve the same physical distance of 13.81 cm between the isocenter and the effective point of measurement. All measurements were performed at a water-equivalent depth of 4 cm.

Campaign	Position 1	Position 2
Campaign 1	IBA PPC05 #475	
	PTW 34001 #2898	
	PTW 34001 #2899	
	PTW 34001 #2460	
	PTW 34045 #2343	
Campaign 2		IBA PPC05 #475 PTW 34001 #2898
Campaign 3	IBA PPC05 #475	IBA PPC05 #475
	PTW 34001 #2898	PTW 34001 #2898
		PTW 34001 #2899
		IBA PPC40 #508
		IBA PPC40 #512
		IBA PPC05 #1632
		IBA PPC05 #1630
		PTW 34045 #2343
		PTW 34045 #2345

Table 7.1: Overview of the ionization chambers used in each measurement campaign and their corresponding positions. IBA PPC05 #475 and PTW 34001 #2898 were included in all campaigns and measurement positions to allow comparison between different datasets. Campaign 2 corresponds to the campaign during which the water and graphite calorimeter measurements were performed.

physical measurement depth of 13.81 cm downstream of isocenter. The graphite calorimeter measurements were performed at the same water-equivalent and physical depth as the water calorimeter measurements, with graphite buildup plates used to achieve a water-equivalent depth of 4 cm. To ensure consistency between detectors, additional ionization chambers measurements were therefore performed by shifting the water phantom such that the effective point of measurement of the chambers was located 13.81 cm downstream of isocenter (position 2). The difference between the physical thickness and the water-equivalent thickness is not identical for all ionization chamber types used. No adjustment of the phantom position was made to account for these small differences, and a constant distance was maintained. However, these differences are below 0.5 mm and are therefore considered negligible compared to the overall positioning uncertainty and included in the uncertainty budget. During the final ionization chamber measurement campaign, several chambers were

measured at both detector positions using the same beam conditions to allow a direct comparison between the measurements obtained at the initial chamber position and those corresponding to the calorimeter measurement geometry. A schematic representation of the different detector positions is shown in figure 7.3, while table 7.1 provides an overview of the measurement campaigns, detector positions, and ionization chambers used.

7.4 Results

7.4.1 Water calorimetry

The correction factors applied to the calorimeter signal, together with the resulting absorbed dose values, are summarized in table 7.2 for the three investigated beam qualities. Table 7.3 presents the uncertainty budget for the determination of absorbed dose to water using the water calorimeter. An example of a calorimeter run in the 284.7 MeV/u beam is shown in figure 7.4.

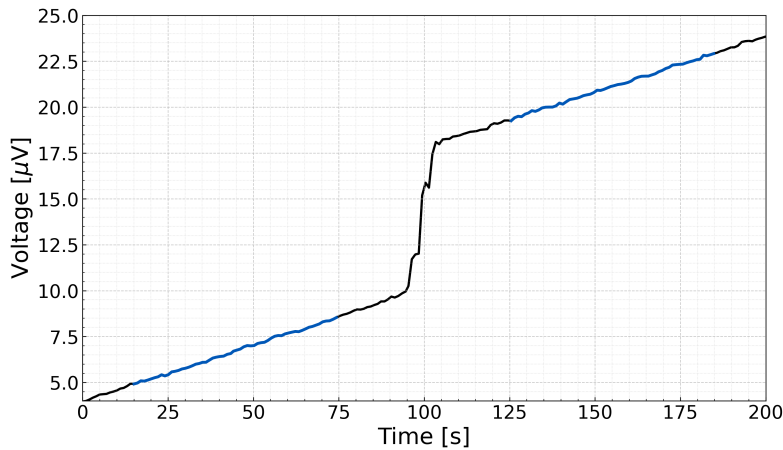


Figure 7.4: Measured water calorimeter signal for the 284.7 MeV/u carbon ion beam. Blue lines show the pre- and post-drift intervals.

A total of 20 runs were performed for the 213.4 and 284.7 MeV/u beams, and 23 runs for the 402.8 MeV/u beam. The resulting standard deviation of the mean was approximately 0.27% for all three energies, which was taken as the type A uncertainty associated with the calorimeter repeatability. All correction factors were close to unity, with deviations below 1%. The largest contribution arises from beam perturbations due to the presence of non-water materials. The perturbation associated with the vessel and thermistor probes results in correction factors slightly smaller than unity, with deviations below 0.3% (see

chapter 6). In contrast, the perturbation due to the calorimeter phantom leads to correction factors larger than unity, with values of approximately 0.9%. Monte Carlo simulations and experimental measurements of this effect agreed within 0.1%. The final perturbation correction factor, k_p was obtained as the product of these two contributions. As the individual uncertainty contributions are similar for the three beam energies, the uncertainty budget presented in table 7.3 is considered representative for all investigated energies. An overall relative standard uncertainty of approximately 0.7% was obtained for the determination of absorbed dose to water using the water calorimeter.

E (MeV/u)	k_c	k_p	k_{HD}	k_ρ	k_{dd}	$D_{w,Q}^{Wcal}$ (Gy)
213.4	1.0008	1.0063	1.0000	0.9996	1.0000	2.068
284.7	1.0021	1.0076	1.0000	0.9999	1.0000	1.564
402.8	0.9996	1.0087	1.0000	1.0000	1.0000	1.229

Table 7.2: Correction factors used for the determination of absorbed dose to water with the water calorimeter and final dose to water values for the three investigated beam qualities.

Quantity	Relative standard uncertainty (%)	Type
Calorimeter repeatability	0.27	A
Thermistor sensitivity	0.07	B
Electronic calibrations	0.20	B
Specific heat capacity c_w	0.05	B
Heat conduction k_c	0.40	B
Beam perturbation k_p	0.22	B
Heat defect k_{HD}	0.30	B
Density correction k_ρ	0.01	B
Beam profile k_{dd}	0.25	B
Positioning	0.10	B
$D_{w,Q}^{Wcal}$	0.70	

Table 7.3: Uncertainty budget associated with the determination of absorbed dose to water using the water calorimeter ($k = 1$).

7.4.2 Graphite calorimetry

The correction factors applied to the graphite calorimeter signal, together with the resulting absorbed dose to water values, are summarized in table 7.4 for

the three investigated beam energies. The corresponding uncertainty budget is presented in table 7.5. Measurements were performed in both isothermal and quasi-adiabatic modes for all beam energies, and the average of the two modes was taken as the final value. Figure 7.5 shows representative calorimeter runs for both the quasi-adiabatic and isothermal modes in the 284.7 MeV/u beam, together with the corresponding radiative energy. For each energy, 20 runs were acquired per mode, except for the 284.7 MeV/u beam, for which only 8 runs were obtained in isothermal mode due to time constraints. The standard deviation of the mean for both modes was approximately 0.2% and was taken as the type A uncertainty associated with the repeatability of the calorimeter measurements. At the time of writing, the correction factors k_{imp} and k_{gap} have not yet been determined for the present beam conditions. Based on previous work in proton beams by Lourenço *et al.*, these factors are expected to be close to unity, and an additional uncertainty contribution was included to account for this assumption. In scattered proton beams, values of $k_{imp} = 1.0016$ and $k_{gap} = 1.0008$ were reported [166]. In scanned proton beams, k_{imp} values between 1.0011 and 1.0017 and k_{gap} values between 0.9997 and 1.0009 were obtained [167]. For the conversion from absorbed dose to graphite to absorbed dose to water ($s_{w,g}k_{fl}$) values of 1.1200, 1.1207 and 1.1196 were obtained for the 213.4, 284.7 and 402.8 MeV/u beams, respectively. These values are consistent with those reported for proton beams in the work of Lourenço *et al.* [166, 167]. The uncertainty associated with these conversion factors is still under evaluation for the specific irradiation conditions used in this work. Therefore, an estimation was made based on the results reported by Lourenço *et al.*, combining the uncertainty determined for k_{fl} factors in carbon ion beams [175] with the uncertainty on $s_{w,g}$ in proton beams [166]. An overall uncertainty of 0.92% was preliminary obtained for the determination of absorbed dose to water using the graphite calorimeter.

E (MeV/u)	k_{imp}	k_{gap}	$s_{w,g}k_{fl}$	$k_{z,cal}$	$D_{w,Q}^{Gcal}$ (Gy)
213.4	1.0000	1.0000	1.1200	1.0000	2.044
284.7	1.0000	1.0000	1.1207	1.0000	1.541
402.8	1.0000	1.0000	1.1196	1.0000	1.214

Table 7.4: Correction factors used for the determination of absorbed dose to water with the graphite calorimeter and final dose to water values for the three investigated beam qualities.

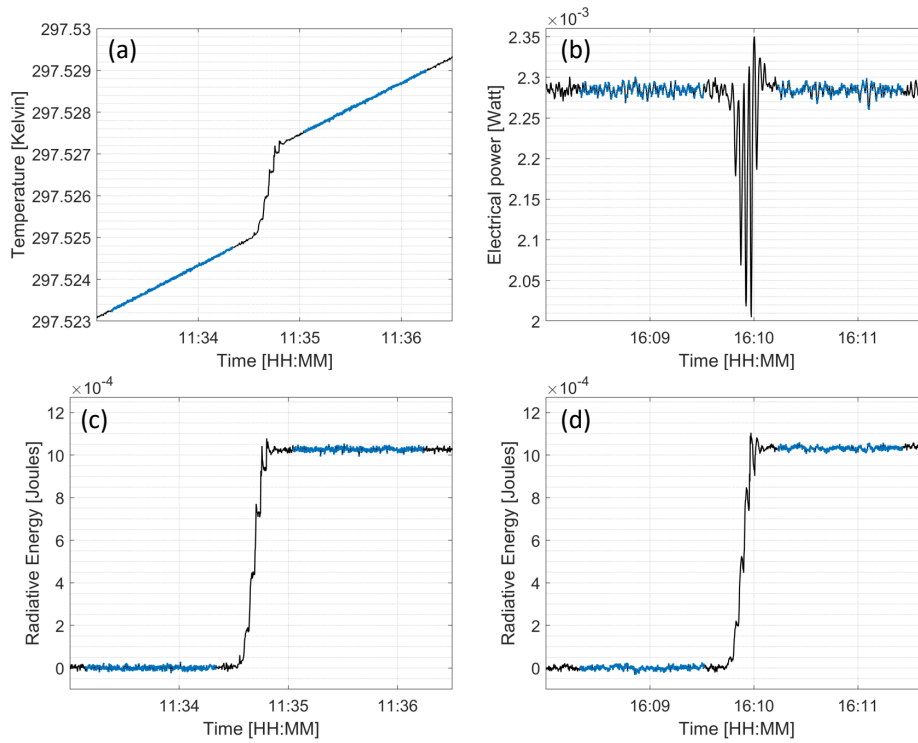


Figure 7.5: Graphite calorimeter runs for the 284.7 MeV/u carbon ion beam: (a) quasi-adiabatic mode and (b) isothermal mode, together with the corresponding radiative energy (c) and (d). Blue lines show the pre- and post-drift intervals. The plots were provided by NPL.

Quantity	Relative standard uncertainty (%)	Type
Repeatability QA mode	0.20	A
Repeatability ISO mode	0.20	A
Analysis	0.15	B
Heat transfers	0.41	B
Electrical calibrations	0.21	B
Specific heat capacity c_g	0.27	B
$k_{imp}k_{gap}$	0.20	B
$s_{w,g}k_{fl}$	0.61	B
$k_{z,cal}$	0.10	B
Reference depth	0.13	B
Graphite mass & impurities	0.09	B
$D_{w,Q}^{Gcal}$	0.92	

Table 7.5: Uncertainty budget associated with the determination of absorbed dose to water using the graphite calorimeter ($k = 1$).

7.4.3 Ionometry

The ion recombination correction factors were small for all ionization chambers and beam conditions. The largest correction was observed for the PTW 34001 chamber, for which the recombination amounted to 0.36%. The uncertainty budget for the determination of absorbed dose to water with the ionization chambers is presented in table 7.6. As discussed previously, the dominant contribution to the uncertainty on the determination of absorbed dose to water using these ionization chambers arises from the k_Q -factor, for which an uncertainty of 2.4% is assigned. When combined with the other uncertainty components, this results in an estimated standard uncertainty of approximately 2.5% on the absorbed dose to water determined with the different ionization chamber types.

7.5 Discussion

Figures 7.6, 7.7, and 7.8 compare the absorbed dose to water values obtained with the water calorimeter, graphite calorimeter, and ionization chambers for the 213.4, 284.7 and 402.8 MeV/u carbon ion beams, respectively.

Two ionization chambers (IBA PPC05 #475 and PTW 34001 #2898) were measured under identical conditions in position 1 during campaigns 1 and 3. For both chambers, the results obtained in the two campaigns agree within

Quantity	Relative standard uncertainty (%)	Type
IC repeatability	0.25	A
Temperature-pressure k_{tp}	0.07	B
Polarity k_{pol}	0.23	B
Ion recombination k_s	0.15	B
Electrometer k_{elec}	0.1	B
Positioning	0.10	B
Beam quality correction k_Q	2.4	B
Calibration coefficient N_{D,w,Q_0}	0.65	B
$D_{w,Q}^{ion}$	2.52	

Table 7.6: Uncertainty budget associated with the determination of absorbed dose to water using the ionization chambers ($k = 1$).

0.4%. The same chambers were also measured in position 2 during campaigns 2 and 3 under identical conditions, showing agreement within 0.2%. These results demonstrate good reproducibility between measurement campaigns performed at different times. Consequently, measurements obtained with other chambers during campaigns 1 and 3 can be reliably compared with the calorimetry data acquired during campaign 2. Measurements obtained in position 1 were corrected to the geometry corresponding to position 2. This correction was derived from measurements performed with two ionization chambers in both positions during campaign 3, and the average ratio between the two positions was applied to adjust the position 1 data.

For each ionization chamber type, two or three individual units were investigated, allowing an assessment of chamber-to-chamber variability. For all chamber types, the agreement remains within 0.4% across all investigated beam energies, indicating low variability between chambers of the same type. The mean absorbed dose to water for each chamber type is also indicated in the figures.

For the three investigated beam energies, the absorbed dose to water obtained with the water calorimeter was systematically slightly higher than with the graphite calorimeter. The differences were 1.2%, 1.5%, and 1.2% for the 213.4, 284.7, and 402.8 MeV/u beams, respectively. Although the graphite calorimeter results are preliminary and some correction factors are still under evaluation, the magnitude of these corrections is expected to be small and is therefore unlikely to substantially affect the observed agreement. Even so, the product

$k_{imp}k_{gap}$ is expected to be slightly greater than unity, which would improve the observed agreement.

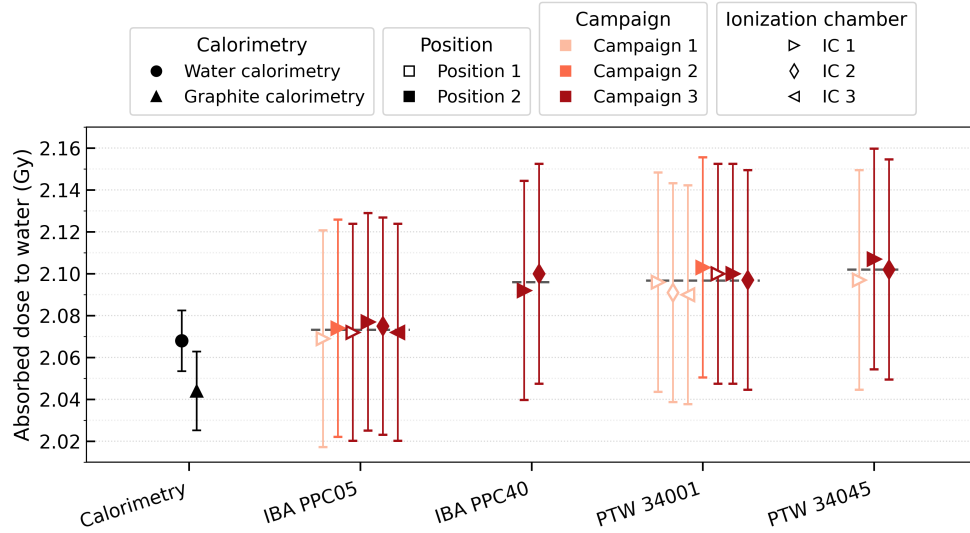


Figure 7.6: Absorbed dose to water determined using the water calorimeter, graphite calorimeter, and ionization chambers in the 213.4 MeV/u carbon ion beam. Data from chambers originally measured in position 1 were corrected to position 2. Measurements performed in position 1 are shown with hollow markers, while measurements in position 2 are shown with filled markers. The three measurement campaigns are distinguished by color. The same marker type represents measurements with the same ionization chamber, while different markers indicate additional units of the same chamber type. Dashed lines indicate the mean value for each chamber type. Error bars represent standard uncertainties ($k = 1$).

The dominant contribution to the uncertainty arises from the conversion of dose to graphite to dose to water, which is obtained through Monte Carlo simulations. This conversion factor is on the order of 12%, with an associated uncertainty of approximately 0.6%, and was calculated using the FLUKA Monte Carlo code. It should be noted that this correction may to some extent depend on the Monte Carlo model employed. Previous work by Stolzenberg *et al.* has reported statistically significant differences in k_Q -factors for carbon ion beams calculated using different Monte Carlo codes, such as GATE and FLUKA, which were attributed to differences in the implementation of nuclear interaction models [102]. As such, a certain degree of code dependence in the graphite-to-water conversion cannot be excluded and may contribute, at least in part, to

the observed differences between the graphite and water calorimeter results.

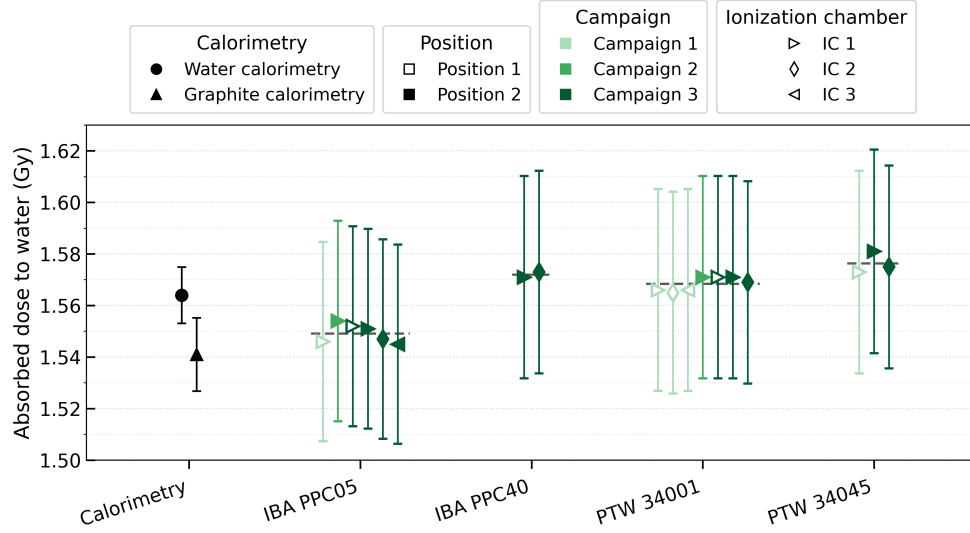


Figure 7.7: Same representation as figure 7.6 for the 284.7 MeV/u carbon ion beam.

For the ionization chambers, it should be noted that the k_Q values recommended in TRS-398 Rev. 1 are not based on the same type of data for all chamber types. For the IBA PPC05, IBA PPC40, and PTW 34001 chambers, the recommended values are derived as the average of the calculated values (equation 2.13) and experimental data [99, 155]. In contrast, for the PTW 34045 chamber, the recommended k_Q -factor is solely based on calculations, as there was no experimental data available at the time of publication. As reported in literature, experimentally determined k_Q -factors in carbon ion beams are generally lower than calculated values [99]. This may explain the slightly higher absorbed dose values observed for the PTW 34045 chamber, with the effect being most noticeable at the highest beam energy. The difference between the two calorimeters remains approximately constant across the investigated beam energies. In contrast, the deviation between ionization chamber measurements and calorimetry appears to vary slightly with beam energy, with larger deviations observed at the lowest energy. The largest deviations are observed for the PTW 34045 chamber in the 213.4 MeV/u beam, amounting to approximately 1.6% relative to the water calorimeter and up to 2.8% relative to the graphite calorimeter. This trend may indicate a weak dependence of k_Q on beam quality, however, further measurements would be required to confirm such a trend. It should also be noted that, for the lowest investigated energy

(213.4 MeV/u, $R_{80} = 90$ mm), the dose gradient at 4 cm depth is steeper than for the higher-energy beams, making the measurements more sensitive to positioning uncertainties and potentially contributing to the larger observed deviations.

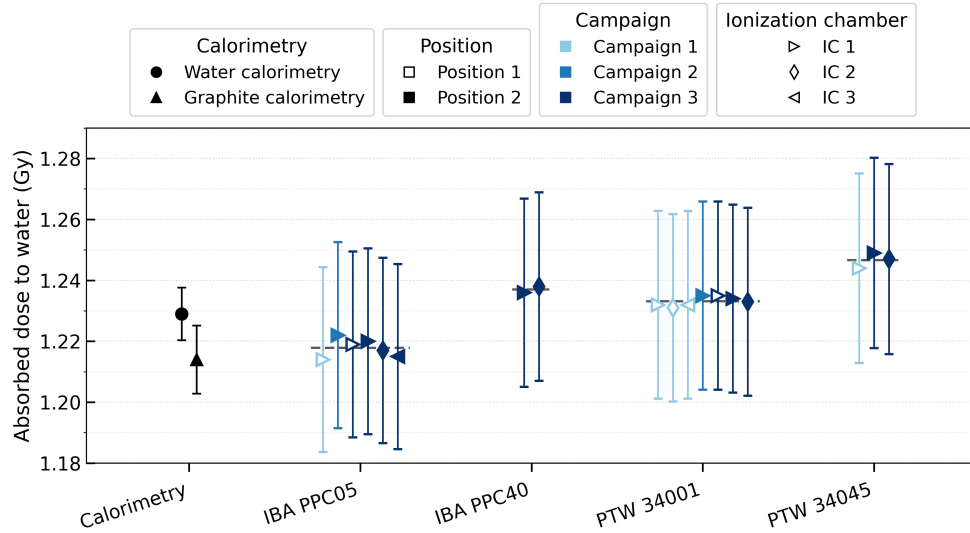


Figure 7.8: Same representation as figure 7.6 for the 402.8 MeV/u carbon ion beam.

7.6 Conclusion

In this work, a direct comparison was performed between the UCLouvain water calorimeter and the NPL graphite calorimeter in the plateau region of scanned carbon ion beams with nominal energies of 213.4, 284.7, and 402.8 MeV/u. To the best of our knowledge, this is the first direct comparison between water and graphite calorimetry in carbon ion beams under identical beam conditions. For all three beam energies, the absorbed dose to water values obtained with the two calorimeters were in agreement within their respective uncertainties. The water calorimeter yielded systematically higher values, with differences of 1.2-1.5%. Although some graphite calorimeter correction factors are still under evaluation, their expected magnitude is small and therefore unlikely to significantly affect this preliminary agreement. The ionization chamber measurements showed good reproducibility between campaigns and low chamber-to-chamber variability, with agreement between individual units within 0.4% for all investigated chamber types. Overall, this work provides an important experimental comparison between independent calorimetric techniques in carbon ion beams.

The observed agreement between water and graphite calorimetry supports the consistency of these approaches and provides additional confidence in absorbed dose to water determinations in this modality.

Chapter 8

Discussion, conclusion and outlook

8.1 Aim and overall contributions

The primary objective of this thesis was to improve the accuracy of reference dosimetry and reduce the uncertainties associated with the determination of absorbed dose to water, particularly in hadron therapy, through the application of water calorimetry. This objective was addressed through four main scientific contributions.

First, several compact cylindrical and plane-parallel ionization chambers were assessed for their suitability as reference dosimeters in high-energy photon beams. For these chambers, beam quality correction factors were determined experimentally using water calorimetry, and their stability and correction factors were evaluated. For some chamber types, these measurements provide the first experimental k_Q data available.

Second, beam quality correction factors were experimentally determined in scanned proton beams for multiple ionization chamber types commonly used in clinical practice. These measurements expand the currently limited experimental database of k_Q -factors and provide validation of the current TRS-398 Rev. 1 recommendations for proton beams.

Third, beam quality correction factors were determined in scanned carbon and helium ion beams. In particular, this thesis presents the first experimental k_Q -factors ever reported for helium ion beams. Together with the extended dataset for carbon ions, these results provide a much-needed experimental basis for reference dosimetry in light ion beams, where protocol uncertainties are currently largest.

Finally, a direct comparison was performed between the UCLouvain water calorimeter and the NPL graphite calorimeter in carbon ion beams. This comparison between two independent calorimetric standards provides an important experimental validation of absorbed dose to water measurements in carbon ion beams.

Taken together, the results of this thesis highlight the key role of calorimetry in benchmarking and improving reference dosimetry for particle therapy, while providing new experimental data to support future refinement of international dosimetry protocols.

The discussion presented in this chapter is not structured strictly according to the individual scientific contributions described above, but rather around broader questions arising from the results. More specifically, it is organized

around five main topics: the impact of the determined k_Q -factors on uncertainty in reference dosimetry, the significance of the comparison between the water and graphite calorimeters, the chamber-to-chamber variability and validity of generic chamber-type k_Q -factors, the possible role of chamber positioning in the discrepancies between Monte Carlo and experimental results, and the potential implications of these discrepancies for the W_{air} value in carbon and helium ion beams. Finally, the possible clinical impact of the findings of this thesis is discussed.

Impact on uncertainties in reference dosimetry

As introduced in chapter 2, the relative standard uncertainty associated with the determination of absorbed dose to water using the $N_{D,w}$ -formalism, as described in TRS-398 Rev. 1, varies considerably across radiation modalities. The dominant contribution to this variation arises from the uncertainty assigned to the beam quality correction factors, k_Q .

For high-energy photon beams (chapter 4), a relative standard uncertainty of 0.6% is associated with the k_Q -factors given in TRS-398 Rev. 1, resulting in an overall uncertainty of approximately 1% on the absorbed dose to water under reference conditions. The k_Q -factors obtained in this work in high-energy photon beams exhibit uncertainties ranging from 1.07 to 1.50%. These values are higher than the uncertainties assigned in TRS-398 Rev. 1 and therefore do not lead to a reduction of the overall uncertainty on absorbed dose to water. This is mainly attributed to the vessel configuration, which resulted in a large heat transfer correction and therefore introduced additional uncertainty. Nevertheless, this work provides the first experimental k_Q values for the IBA RAZOR™ Nano chamber. Despite the larger uncertainties, the obtained values agree with available Monte Carlo and experimental data for most chamber types. Therefore, these results support the use of generic k_Q -factors for these chamber types in high-energy photon beams while expanding the available experimental database. In addition, these small-volume chambers may be particularly relevant for techniques such as FFF beams and GRID therapy, where high spatial resolution is required.

In proton beams (chapter 5), TRS-398 Rev. 1 assigns a relative standard uncertainty of 1.4% to the k_Q -factors, based on the work of Palmans *et al.* [141]. This results in an overall uncertainty of approximately 1.7% on the absorbed dose to water. The k_Q -factors obtained in this work have uncertainties ranging from 0.8% to 1.5%, depending on the chamber type and calorimeter vessel configuration. When using the optimized vessel configuration with reduced

heat transfer corrections, the uncertainty on the k_Q -factors can be reduced by approximately 0.6% compared to the values currently recommended in TRS-398 Rev. 1. Propagating this improvement through the $N_{D,w}$ -formalism results in a decrease of the overall uncertainty on absorbed dose to water from approximately 1.7% to about 1.2%. For chamber types where the obtained uncertainties were slightly higher, the results remain consistent with the protocol values. For comparison, the IPEM Code of Practice for proton therapy dosimetry reports a relative standard uncertainty of approximately 1.0% on the absorbed dose to water, based on the NPL Proton Primary Standard graphite calorimeter, by determining the absorbed dose directly in the user beam [168].

For carbon and helium ion beams (chapter 6), TRS-398 Rev. 1 does not distinguish between ion species and assigns an uncertainty of 2.4% to the generic k_Q -factor for all light ions. This results in an overall uncertainty on the absorbed dose to water of approximately 2.7% under reference conditions. Such a value is substantial, particularly given that additional uncertainties arise from treatment planning, beam delivery, imaging and patient positioning, while recommended total clinical uncertainties aim to remain below 5% and preferably around 3.5% [4, 5]. In this work, the experimentally determined k_Q -factors for carbon and helium ion beams exhibit relative standard uncertainties ranging between 0.7% and 1.3%, depending on the chamber type. These values are approximately a factor of two lower than the uncertainty currently assigned in TRS-398 Rev. 1. Incorporating these improved uncertainties into the dose determination would therefore result in overall uncertainties between 1.3% and 1.7%.

Significance of water and graphite calorimeter comparison

The direct comparison between the water calorimeter and the NPL graphite calorimeter provides an important cross-validation between two independent calorimetric dosimetry systems in carbon ion beams. To the best of our knowledge, this work represents the first direct experimental comparison between water and graphite calorimetry in this modality.

For the three investigated beam energies, the absorbed dose to water values obtained with both calorimeters differed by approximately 1.2-1.5%. These results are preliminary, as some correction factors for the graphite calorimeter are still under evaluation. However, their expected magnitude is small and is therefore unlikely to substantially alter this level of agreement, with a slight improvement anticipated. This agreement strengthens confidence in the realization of absorbed dose to water in carbon ion beams and provides additional

validation of the absorbed dose values determined with the water calorimeter in this work. Furthermore, these findings suggest that the discrepancies observed between Monte Carlo and experimental k_Q -factors based are unlikely to originate from the water calorimetric determination of absorbed dose as a technique, and are therefore more likely related to modeling assumptions or underlying physical parameters.

Chamber-to-chamber variability and validity of generic k_Q -factors

TRS-398 Rev. 1 recommends using chamber-specific k_Q values whenever available. In practice, however, such data are rarely available, particularly for hadron therapy beams, as primary and secondary standards laboratories are currently not equipped with proton, carbon or helium ion beams. Consequently, the protocol provides generic k_Q -factors per chamber type, implicitly assuming negligible chamber-to-chamber variability.

In this work, several chambers of the same type were measured under identical experimental conditions in order to investigate this variability. For most chamber types, the observed chamber-to-chamber variability was limited. In photon beams, differences remained below 0.2% for the chamber types tested. In proton beams, differences of approximately 0.2% were observed for the IBA PPC40 chamber and about 0.5% for the IBA PPC05 chamber. In carbon ion beams, chamber-to-chamber variability remained limited for most chamber types, with differences generally below 0.4%. However, larger differences of up to 1.3% were observed for one of the IBA PPC05 chambers. A similar trend was observed for the same chamber in helium ion beams, where a difference of approximately 1% was measured, but variability remained below 0.4% for all other chamber types tested.

Previous investigations have also examined the potential influence of small manufacturing differences on the resulting k_Q -factors. Houyoux *et al.* evaluated this effect in proton beams using Monte Carlo simulations and concluded that realistic variations in chamber geometry are expected to have only a limited impact on the k_Q values [176]. The variability observed in the present work is generally consistent with this conclusion. However, the larger deviation observed for one of the PPC05 chambers suggests that, for this chamber type, the influence of such variations may be more pronounced than previously assumed. The PPC05 is a small volume ionization chamber (electrode spacing 0.6 mm) compared to Roos-type and Farmer-type chambers, which may increase its sensitivity to small manufacturing differences. Increased variability in k_Q -factors has also been reported for other small volume chambers, such as pinpoint-type

chambers, with differences up to 2% in photon beams and around 1% in proton beams [177].

Overall, the results indicate that the use of generic k_Q -factors per chamber type is a reasonable approximation for most ionization chambers investigated in this work. Nevertheless, the larger variability observed for the PPC05 chamber suggests that chamber-specific k_Q -factors may be preferable for this chamber type.

Monte Carlo–experimental discrepancies: the role of chamber positioning

Independent dosimetry audits in proton therapy centers have reported larger deviations when using the IBA PPC05 chamber compared to other ionization chamber types. Carlino *et al.* observed deviations of up to 2.7% in centers using the PPC05 chamber, whereas differences remained within approximately 1.5% when using other chamber types such as Farmer or Roos chambers [178]. Similarly, Vilches-Freixas *et al.* compared the IBA PPC05, PTW 34001, PTW 34045 and PTW 30012 chambers in proton beams and observed systematically lower absorbed dose values when using the IBA PPC05 chamber [179]. In both studies, the k_Q -factors recommended in TRS-398 Rev. 1 were used and the chambers were positioned using the water-equivalent thickness of the entrance window.

A possible explanation for this behavior has been proposed based on the positioning of plane-parallel ionization chambers. In TRS-398 Rev. 1 it is recommended that plane-parallel chambers are positioned using the water-equivalent thickness of the entrance window. In Monte Carlo simulations, however, this is not always taken into account and chambers are often positioned using the physical thickness of the entrance window. For most commercially available plane-parallel chambers, the water-equivalent thickness closely approximates the physical thickness, making this difference negligible. For the PPC05 chamber, however, the difference is substantial, with a physical thickness of approximately 1 mm and a water-equivalent thickness of about 1.6 mm. As a result, when positioning the chamber using the physical thickness rather than the WET, the effective measurement depth is slightly shifted, which may lead to differences, particularly in regions where dose gradients are present. Baumann *et al.* investigated this effect and showed that for most chambers the impact is negligible, whereas for the IBA PPC05 chamber deviations of up to approximately 0.5% may occur [150].

In the present work, the ionization chambers were positioned taking into

account the water-equivalent thickness of the entrance window. The experimentally determined k_Q values for the IBA PPC05 chamber in proton beams were found to be higher than the value recommended in TRS-398 Rev. 1 for all three PPC05 chambers investigated. Using these experimentally determined values instead of the TRS-398 Rev. 1 value would reduce the discrepancies observed in the studies of Carlino *et al.* [178] and Vilches-Freixas *et al.* [179] by approximately 0.8–1.4%, leading to much better agreement with the other ionization chamber types.

An interesting observation is that Monte Carlo-based k_Q -factors reported in literature generally predict similar values for the IBA PPC05 and PPC40 chambers across different ion beam modalities. For proton beams, Monte Carlo calculations yield values of approximately 0.992 for the PPC05 and 0.995 for the PPC40 chamber. In carbon ion beams, Houyoux *et al.* (submitted) reported values of approximately 1.012 for both chambers, while for helium ion beams values of approximately 1.006 and 1.007 were obtained. In all cases, the predicted differences between the PPC05 and PPC40 chambers are negligible.

In contrast, the experimental results obtained in this work show a systematic difference between these two chamber types across all investigated modalities. Differences between the PPC05 and PPC40 chambers range from approximately 1% up to 3% in proton, carbon and helium ion beams. Although the PPC05 chambers exhibit a larger chamber-to-chamber variability, the results consistently indicate a systematic difference between the PPC05 and PPC40 chambers that is not reproduced by current Monte Carlo simulations. In proton beams, part of this discrepancy may be attributed to positioning effects as discussed above. However, under the experimental conditions investigated in this work, dose gradients in the plateau region of carbon ion beams are relatively small, and positioning effects are therefore expected to be limited. The persistence of discrepancies across proton, carbon and helium ion beams therefore suggests that additional factors may be involved, such as aspects of the chamber modeling that may not yet be fully captured in current Monte Carlo simulations.

Furthermore, inconsistencies exist in the literature regarding how plane-parallel ionization chambers are positioned in both experimental measurements and Monte Carlo calculations. Although TRS-398 Rev. 1 recommends positioning based on the water-equivalent thickness of the entrance window, this approach is not consistently applied in Monte Carlo studies. For example, Houyoux *et al.* (submitted) considered the water-equivalent thickness, whereas Urago *et al.* [100] and Stolzenberg *et al.* [102] positioned the chambers using the physical thickness. Although the impact of this difference is expected to be small for most

chambers, particularly in beams with small dose gradients, it would nevertheless be desirable to establish a clear consensus on the positioning methodology in order to avoid ambiguities. Additional experimental data will also be important to further validate the Monte Carlo-determined k_Q values for these chambers.

Monte Carlo–experimental discrepancies: the role of W_{air}

While experimental and Monte Carlo results generally agree for most ionization chamber types in proton beams, larger discrepancies are observed in light ion beams. In carbon ion beams, differences of approximately 1–3% are typically reported, with Monte Carlo-calculated k_Q values being consistently higher than the experimentally determined values. A similar trend, although somewhat smaller, is observed for helium ion beams. These discrepancies appear consistently across different independent studies and Monte Carlo codes, suggesting that a common input parameter in the simulations may be responsible for the observed differences.

One possible factor contributing to these discrepancies is the mean energy required to produce an ion pair in air, W_{air} . At present, the uncertainty associated with W_{air} represents the dominant contribution to the overall uncertainty in Monte Carlo-determined k_Q values for light ion beams. The value currently recommended in ICRU report 90 and used in TRS-398 Rev. 1 for the calculation of k_Q -factors for light ions is 34.71 eV, with a standard uncertainty of 1.5% [75]. In contrast, for proton beams the uncertainty associated with W_{air} is substantially smaller, approximately 0.4%, based on the work of Andreo [180]. This difference may partly explain why Monte Carlo and experimental k_Q values generally show better agreement in proton beams than in light ion beams.

Using the experimental results obtained in this work, approximate W_{air} values can be estimated for the investigated beam modalities. This can be done by combining the experimentally determined k_Q values with the stopping power ratios $(s_{w,air})_Q$ used in TRS-398 Rev. 1 and assuming the perturbation factors p_Q to be unity in equation 2.13. For the reference beam quality, the values of $(s_{w,air})_{Q_0}$, W_{air,Q_0} , and p_{Q_0} recommended in TRS-398 Rev. 1 were used. The resulting W_{air} values were then averaged over all chamber types investigated in this work. This approach yields estimated W_{air} values of approximately 34.15 eV for helium ion beams and 34.04 eV for carbon ion beams. These values are lower than the currently recommended value of 34.71 eV, corresponding to reductions of up to approximately 2%.

An alternative estimate can be obtained by combining the experimental k_Q -

factors measured in this work with the f_Q -factors reported in several Monte Carlo studies [100–102]. Using the average f_Q values from these studies results in estimated W_{air} values of approximately 34.17 eV for helium ions and 34.00 eV for carbon ions. These values are again lower than the currently recommended value and are in good agreement with the estimates obtained under the assumption that $p_Q = 1$.

A similar trend has been reported in the work of Holm, who derived a value of approximately 33.96 eV for carbon ions based on water calorimetry measurements [160]. In contrast, two other studies have attempted to determine W_{air} values in carbon ion beams using graphite calorimetry measurements. Rossomme *et al.* [170] reported a value of 35.5 eV, while Sakama *et al.* [169] reported a value of 35.72 eV, corresponding to values approximately 3% higher than the value recommended in ICRU Report 90. However, since the graphite calorimeter of NPL showed good agreement with the water calorimeter used in this work, the observed differences are unlikely to originate from systematic discrepancies between graphite and water calorimetry techniques. It is worth noting that the absorbed dose to water values obtained with the graphite calorimeter were systematically lower than those obtained with the water calorimeter, which would in turn lead to a lower estimated W_{air} value.

The W_{air} values derived for helium and carbon ion beams in this work are consistent with the hypothesis proposed by Dennis [181] and later reiterated by Verhey and Lyman [182], that as particle energies increase toward the relativistic regime, the W_{air} value becomes independent of the charged particle type. In this regime, ionization is increasingly dominated by secondary electrons, such that W_{air} approaches the value for electrons in air, estimated to be approximately 33.97 eV [75].

Although these estimates should be interpreted with caution, they suggest that the effective W_{air} value for light ion beams may be lower than the value currently used in dosimetry protocols. If confirmed, such a reduction could explain the systematic discrepancies observed between Monte Carlo and experimentally determined k_Q -factors for helium and carbon ion beams. However, an accurate experimental determination of W_{air} requires reliable knowledge of stopping power ratios $s_{w,air}$ and chamber perturbation factors, which are still insufficiently characterized for light ion beams. Further coordinated experimental and modeling work will therefore be required before definitive conclusions can be drawn regarding the appropriate value of W_{air} for helium and carbon ion beams.

Clinical impact

From a clinical perspective, uncertainties in absorbed dose directly translate into uncertainties in treatment outcome. Both the tumor control probability and the normal tissue complication probability depend strongly on the delivered dose, such that even small variations can lead to measurable changes in predicted outcome. This sensitivity is particularly pronounced in regions where the dose-response curve is steep. The clinical relevance of such variations has been quantified by Bolt, who showed that reducing the standard deviation of delivered dose from 0.8% to 0.4% can decrease the variability in predicted TCP values by up to 3.7% for an individual patient and by up to 2% at the population level [183].

In addition, systematic differences in delivered dose can have an even greater impact. For example, a systematic shift of $\pm 2\%$ in dose has been shown to significantly alter the number of patients achieving high TCP values ($> 90\%$), with changes on the order of thousands of patients in large cohorts [183]. In this context, the experimentally determined k_Q -factors for light ion beams in this work are approximately 2% lower than the values currently recommended in TRS-398 Rev. 1. Since the absorbed dose to water is directly proportional to k_Q , the use of these experimental values would lead to a corresponding change in the dose of approximately 2%.

These findings indicate that improvements in dosimetric accuracy, such as the reduction in uncertainty from approximately 2.7% to 1.3-1.7% for light ion beams demonstrated in this work, may reduce variability in treatment outcome. At the same time, systematic differences in k_Q -factors may introduce clinically relevant shifts in delivered dose. Together, this highlights the importance of accurate and experimentally validated beam quality correction factors for ensuring both treatment efficacy and patient safety in particle therapy.

8.2 Limitations and future perspectives

Several limitations of the present work should be acknowledged, as they may influence the interpretation of the results or indicate directions for future improvements. The following section briefly discusses these limitations and outlines possible avenues for future research.

Number of ionization chambers

First, although the number of ionization chambers investigated in this work is larger than in several previous studies, it remains relatively limited. A large

number of chamber types commonly used in clinical practice were not included in this study. Furthermore, for the chamber types that were investigated, the number of units per type was generally small. At most, four chambers of the same type were measured within the same beam modality, while for several chamber types only one detector was available. In such cases, no conclusions can be drawn regarding possible chamber-to-chamber variability. For other chamber types, only two chambers were tested, which still provides limited statistical insight into manufacturing variability. Consequently, the present results provide only a partial indication of chamber-to-chamber variability and the validity of generic k_Q -factors for different chamber types. A more comprehensive assessment would require measurements of a larger number of detectors for each chamber type. In addition, some of the investigated chambers had close serial numbers, such as the IBA PPC40 #508 and #512, PTW 34001 #2898 and #2899, and IBA PPC05 #1630 and #1632. These chambers likely originate from the same manufacturing batch, which may reduce the observed variability. Future studies including chambers from a wider range of production batches would therefore provide a more representative evaluation of chamber-to-chamber differences.

Cobalt-60 calibration coefficients

In this work, the k_Q -factors were derived using calibration coefficients in the user beam determined experimentally through water calorimetry, while the calibration coefficients in the reference beam (N_{D,w,Q_0}) were obtained from Secondary Standards Dosimetry Laboratories. Although these calibration coefficients are traceable to primary standards, in some cases realized using water calorimetry, they introduce an additional uncertainty component compared to a situation where both calibration coefficients are determined directly using the same calorimetric system. In the work of Wang *et al.* [145] and Holm *et al.* [160], for example, the calibration coefficients in the reference ^{60}Co beam were determined using the same water calorimeter system that was used for the measurements in proton and carbon ion beams. In these studies, they reported standard uncertainties of approximately 0.25% on N_{D,w,Q_0} , whereas the calibration coefficients used in the present work have associated uncertainties between 0.5% and 1.1%, depending on the SSDL and chamber. Determining the ^{60}Co calibration coefficients directly with the same water calorimeter could therefore potentially reduce the uncertainty associated with the determined k_Q -factors. In addition to the lower uncertainty on the calibration coefficient itself, determining both coefficients with the same calorimeter would introduce correlations between several uncertainty components. These correlations would lead to partial cancellation of common uncertainty contributions in the ratio

defining the k_Q -factors, further reducing the overall uncertainty.

Heat transfer correction

One of the most important correction factors applied in water calorimetry is the heat transfer correction, which accounts for conductive heat transfer in the water. Two limitations related to this correction in the present work should be noted. First, during some of the early measurement campaigns a vessel configuration was used that resulted in a relatively large heat transfer correction, introducing larger uncertainties in the determination of absorbed dose. In later campaigns, an improved vessel design was implemented, resulting in substantially smaller heat transfer corrections. For future measurements, the use of this vessel configuration is therefore preferred in order to minimize the magnitude of the correction and the associated uncertainty. Second, the finite element simulations used to determine the heat transfer correction were implemented using a simplified temporal structure of the scanned beams. The spot-scanning time structure was not modeled spot-by-spot. Instead, the beam delivery was approximated either as a sequence of spills or, when the delivery time was short, as an instantaneous delivery of the full field. These simplifications were introduced to reduce the computational complexity and time of the finite element simulations. Although this approach allowed the heat transfer correction to be evaluated efficiently, a more detailed modeling of the spot-scanning time structure could provide a more accurate representation of the irradiation conditions.

The heat defect

The calorimeter vessel in this work was prepared by filling it with ultrapure water and saturating it with hydrogen, followed by a pre-irradiation procedure in order to minimize the heat defect. Hydrogen-saturated water calorimetry systems have been extensively studied for low-LET radiation; however, fewer investigations have been performed for higher-LET radiation such as carbon ion beams. Sassowsky and Pedroni [147] calculated that for LET values up to approximately $25 \text{ keV } \mu\text{m}^{-1}$, a stationary chemical state is achieved in hydrogen-saturated water, resulting in a zero net heat defect. In the present work, the LET of the beams used for the measurements was not explicitly determined. In the work of Osinga-Blättermann *et al.* [154], a maximum LET value of about $11.3 \text{ keV } \mu\text{m}^{-1}$ was determined in the plateau region of a 429 MeV/u carbon ion beam, while Holm [160] reported a maximum LET value of approximately $31.56 \text{ keV } \mu\text{m}^{-1}$ in the SOBP of a carbon ion beam. In addition, Khan *et al.* reported LET values between approximately 11 and $22 \text{ keV } \mu\text{m}^{-1}$ in the plateau

region of monoenergetic carbon ion beams with energies ranging from 150 to 450 MeV/u [156]. In this work, measurements were performed in the plateau region of carbon ion beams with nominal energies ranging from 213.4 to 402.8 MeV/u, and therefore the corresponding LET values are expected to remain below those reported for the SOBP measurements. Consequently, it seems reasonable to assume that the LET values in the present measurements do not exceed the range for which the hydrogen-saturated system is expected to reach a stationary chemical state, and the heat defect is therefore assumed to be negligible.

Nevertheless, a direct determination of the LET under the present beam conditions, or dedicated investigations of the heat defect in higher-LET carbon ion beams, would be valuable to further confirm this assumption. It is worth noting that both Osinga-Blättermann *et al.* [154] and Holm [160] also employed a hydrogen-saturated system and assumed a zero heat defect in their work. Finally, the agreement observed between the absorbed dose measurements obtained with the water calorimeter and those obtained with the graphite calorimeter suggests that this assumption is likely valid under the present experimental conditions. However, further experimental studies could provide additional confirmation, particularly for measurements performed in the SOBP region, where LET values are higher.

LET dependence and SOBP measurements

All measurements reported in this work were performed in the plateau region of the investigated beams and therefore do not address the potential LET dependence of the k_Q -factors in the SOBP. Only a few studies have investigated this aspect in carbon ion beams. Holm *et al.* reported no significant difference between k_Q values measured in the plateau region and those obtained in the middle of an SOBP created using a 2D range modulator [99]. The Monte Carlo study by Houyoux *et al.* (submitted) predicted slightly larger k_Q -factors in the SOBP compared to the plateau region, although the differences generally remained within approximately 0.6%. Khan *et al.* investigated the LET dependence of f_Q -factors of different ionization chamber types and observed no LET dependence for most chambers. However, for one chamber type a difference up to 0.87% was reported between pristine beams and SBPs, together with a significant LET dependence within pristine beams [156].

Preliminary measurements were also attempted in the SOBP region of a scanned beam within the present study. However, the measurements were not included in the final analysis due to the increased complexity associated with

modeling the scanned beam time structure and the corresponding heat transfer corrections in the calorimetric analysis. Additional exploratory measurements using a 2D range modulator were also performed, but large uncertainties associated with the dose profiles prevented a reliable determination of k_Q -factors. Further studies extending measurements to SOBP conditions would therefore be valuable to further investigate the possible LET dependence of k_Q -factors in carbon ion beams.

Ion recombination

Ideally, the ion recombination correction factor should be determined by measuring full Jaffé plots, which describe the relationship between the inverse of the chamber reading and $1/V$ or $1/V^2$. If linearity is observed in one of these representations, the two-voltage method can be used as an approximation to determine the recombination correction. In this work, full Jaffé plots were not measured due to time constraints, and recombination was instead determined using measurements at two different voltages for each ionization chamber. The two-voltage method for continuous beams was applied for the proton, carbon and helium ion beams used in this work, assuming a linear relationship in $1/V^2$. However, this assumption may slightly underestimate the recombination correction [184, 185]. An additional uncertainty component was therefore included to account for this potential effect. Nevertheless, a more detailed investigation of ion recombination, including full Jaffé plots under the relevant beam conditions, would be valuable to confirm the validity of this assumption.

In addition, the recombination correction was measured for only one chamber of a given type, even when multiple units of the same chamber type were available, and the resulting correction was assumed to apply to the other units. While this assumption is likely reasonable for most chamber types, some chamber-to-chamber variability was observed in the k_Q -factors measured in this work. Small differences in chamber geometry or electrode spacing could therefore also lead to slight differences in recombination behavior.

8.3 Final conclusions

Overall, this thesis demonstrates the important role of calorimetry in improving reference dosimetry for particle therapy and provides new experimental data across several radiation modalities. By combining calorimetric absorbed dose measurements with ionization chamber dosimetry, this work expands the experimental basis of beam quality correction factors and contributes to reducing uncertainties in the determination of absorbed dose to water.

New experimental k_Q -factors were determined for several ionization chamber types in high-energy photon and proton beams, providing additional experimental validation of the recommendations given in TRS-398 Rev. 1. A major contribution of this thesis is the experimental determination of k_Q -factors in carbon and helium ion beams. In particular, this work presents the first experimentally determined k_Q -factors for helium ion beams. The uncertainties obtained for light ions, ranging from approximately 0.7% to 1.3%, are substantially lower than the uncertainties currently assigned in TRS-398 Rev. 1. The results also provide new insight into chamber-to-chamber variability and the discrepancies observed between Monte Carlo and experimental k_Q values. While variability was generally small for most chamber types, a larger deviation was observed for the IBA PPC05 chamber. In addition, the systematic differences between experimental and Monte Carlo results suggest that key parameters used in the calculations, such as the mean energy required to produce an ion pair in air, W_{air} , may require further investigation for light ion beams.

An important experimental validation was achieved through the direct comparison between the water calorimeter used in this work and the NPL graphite calorimeter in carbon ion beams. The absorbed dose values obtained with both systems agreed within the combined standard uncertainties for all investigated beam energies. This first direct comparison between water and graphite calorimetry in carbon ion beams provides strong support for the consistency between two independent realizations of absorbed dose to water.

Finally, this work has demonstrated that a transportable water calorimeter can operate reliably across different radiation modalities, including hadron therapy beams. This opens the possibility of performing absorbed dose calibrations directly at particle therapy facilities, allowing ionization chambers to be calibrated in the user's beam. Such an approach could reduce the reliance on beam quality correction factors and further decrease the uncertainties in clinical dose measurements. Although implementing such a calibration service would require significant effort, the results obtained in this work suggest that it may be feasible in the future.

Ultimately, improving the accuracy of reference dosimetry contributes directly to reducing uncertainties in the dose delivered to patients. By strengthening the experimental foundation of absorbed dose determination in proton and light ion beams, the results presented in this thesis support ongoing efforts to improve the precision and reliability of clinical dose delivery in advanced radiotherapy modalities.

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