Radiation dosimetry of clinical proton beams

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"I can think, I can wait, I can fast"

Siddhartha
Abstract

The aim of this thesis is to improve the accuracy and reduce the uncertainty in the radiation dosimetry of radiotherapy proton pencil beams. Special emphasis is put on the absolute determination of the absorbed dose to water.

To that aim, Monte Carlo simulation techniques were used to calculate cornerstone quantities for the relative and reference dosimetry of proton pencil beams, namely water/medium stopping-power ratios and beam quality correction factors. Monte Carlo calculations were validated with experimental data obtained with ionization chamber and Faraday cup dosimetry. Finally, a novel approach to the reference dosimetry of proton pencil beams based on the concept of ‘dose-area product’ was described and its feasibility assessed.

The Monte Carlo calculation of water/medium stopping-power ratios revealed that the most suitable detection materials for the relative dosimetry of proton pencil beams in water are air and radiochromic film active layer. Lithium fluoride and silicon may also be used for the measurement of lateral dose profiles and field-specific dose distributions in water; whereas the use of gadolinium oxysulfide should be limited to relative dose measurements in air. Concerning reference dosimetry, it appears that the largest source of uncertainty in the water/air stopping-power ratios arises from the uncertainty of the mean excitation energy of water—where an increase of 3 eV results in a decrease of approximately 0.6% in the water/air stopping-power ratios.

The Monte Carlo calculation of beam quality correction factors yielded results which agree within 2.3% with the values tabulated in IAEA TRS-398 Code of Practice, and within 1% with published experimental values obtained with water calorimetry. These results also point at ionization chamber perturbation correction factors in proton beams that may differ significantly from unity.

Reference dosimetry based on IAEA TRS-398 was compared to Faraday cup dosimetry. These two independent dosimetry techniques were found to agree within approximately 3% when using IAEA TRS-398 beam quality correction factors, and within approximately 1.5% when using the Monte Carlo beam quality correction factors calculated in this work. This comparison also pointed at a systematic error in the determination of the absorbed...
dose to water, especially relevant for low-energy proton beams, when using cylindrical ionization chambers together with IAEA TRS-398 reference conditions for monoenergetic proton beams. This error, which arises from the recommendation of positioning the reference point of cylindrical chambers at the reference depth, could be corrected by (i) positioning the effective point of measurement at the reference depth or (ii) including a correction for dose gradient effects in the beam quality correction factors.

Finally, a novel approach to the reference dosimetry of proton pencil beams was described. This approach, based on the determination of the dose-area product of a single proton pencil beam, was shown to be feasible and equivalent to the standard approach based on the determination of the absorbed dose to water at the centre of a uniform broad field.
Zusammenfassung

Das Ziel dieser Doktorarbeit ist es, sowohl die Richtigkeit als auch die Präzision in der Dosimetrie von therapeutischen Protonen-Nadelstrahlen zu erhöhen. Der Fokus liegt dabei auf der absoluten Bestimmung der Wasserenergiedosis.


Die aus den Monte-Carlo-Simulationen gewonnenen Korrektionsfaktoren \( k_Q \) decken sich mit den Literaturwerten: sie stimmen innerhalb von 2.3% mit den tabellierten Werten des IAEA TRS-398 „Code of Practice“ überein und entsprechen kalorimetrisch ermittelten Messwerten innerhalb von 1%. Die Ergebnisse weisen ferner darauf hin, dass Störungskorrektionsfaktoren in Protonenstrahlen erheblich von eins abweichen können.

Referenzdosimetrie nach IAEA TRS-398 Protokoll und absolute Dosimetrie mittels Faraday-Becher stimmen innerhalb von ca. 3% überein, wenn die im Protokoll angegebenen Korrektionsfaktoren \( k_Q \) verwendet werden. Die Abweichungen der beiden unabhängigen Messtechniken dezimieren
sich auf ca. 1.5%, sobald die aus den Monte-Carlo-Simulationen gewonne-
en Korrektionsfaktoren \( k_Q \) zugrunde gelegt werden. Dieser Vergleich weist außerdem auf einen systematischen Fehler bei der Bestimmung der Wasser-
renergiedosis hin, sofern zylindrische Ionisationskammern in Kombination
mit den IAEA TRS-398 Richtlinien für monoenergetischen Protonenstrah-
len verwendet werden. Das Protokoll empfiehlt nämlich den Referenzpunkt
der Kammer in der Referenztiefe zu positionieren. Diese Fehlvorgabe wirkt sich besonders auf die Vermessung niederenergetischer Protonenstrahlen aus
und könnte dadurch behoben werden, dass man entweder (i) den effektiven
Messpunkt der Kammer in der Referenztiefe positioniert, oder (ii) einen zu-
sätzlichen Korrektionsfaktor einführt, der den Einfluss des Dosisgradienten
kompensiert.

Abschließend wurde ein neuartiger Ansatz für die Referenzdosimetrie von
therapeutischen Protonen-Nadelstrahlen erarbeitet. Es konnte gezeigt wer-
den, dass die Bestimmung des „Dosis-Flächen-Produktes“ eines einzelnen
Protonen-Nadelstrahls (Neuansatz) äquivalent zur Bestimmung der Wasser-
renergiedosis im Zentrum eines breiten Protonenfeldes ist (Standardvorge-
hensweise).
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List of publications

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Chapter 1

Introduction

1.1 Background

Cancer figures among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and 8 million cancer-related deaths in 2012 (Stewart & Wild 2014). According to best available evidence, approximately one half of these new cancer patients would require external beam radiation therapy at least once during the course of their disease (Delaney et al. 2005, Delaney & Barton 2015, Borras et al. 2015).

Radiation therapy, or radiotherapy, is a medical treatment modality that uses ionizing radiation with therapeutical purposes. External beam radiation therapy, the most common form of radiation therapy, uses sources of ionizing radiation which are external to the patient body. Amongst the different types of external radiation beams, the so-called ‘high-energy’ photon beams are the most widely used. These photon beams are produced by the bremsstrahlung emission of electron beams, typically in the energy range from 4 to 18 MeV.

Proton therapy is a type of external beam radiation therapy which uses proton beams in the energy range from 50 to 250 MeV. Pioneered by Wilson (1946), proton therapy exploits the physical properties of protons—and their interaction with matter—which allow for a highly localized energy deposition in the human body, as compared to high-energy photon beams. With the emergence of modern delivery (Pedroni et al. 1995, 2004) and treatment planning techniques (Lomax 1999), proton therapy is nowadays capable of delivering superior dose distributions than high-energy photon beams, especially in terms of integral dose to the patient.

Radiation dosimetry is the field of physics that assesses and quantifies the amount of energy absorbed in the human body from ionizing radiation. In the field of radiation therapy, the quantity most frequently used is the absorbed dose (Allisy et al. 1998) and, in particular, the absorbed dose to water. Thus, the radiation dosimetry of radiotherapy beams focuses mainly
on the measurement and determination of the absorbed dose to water. It is of utmost importance that the radiation dosimetry of clinical radiotherapy beams is performed uniformly and consistently throughout the world. In this way, clinical experience can be transferred between different radiotherapy centres and the treatment outcome of different radiotherapy modalities can be compared.

The radiation dosimetry of external radiotherapy beams is described in two consensus documents: AAPM TG-51 dosimetry protocol (Almond et al. 1999)—which deals with high-energy photon and electron beams—and IAEA TRS-398 Code of Practice (Andreo et al. 2000)—which includes all types of external radiotherapy beams. Both documents are based on the same formalism and standards of absorbed dose to water (see section 2.2.4). For clinical proton beams, a third consensus document, ICRU Report No. 78 (Jones et al. 2007), also recommends the adoption of IAEA TRS-398 Code of Practice.

The determination of the absorbed dose to water in clinical proton beams is subject to a larger uncertainty than in high-energy photon beams. This uncertainty propagates inevitably to all clinical studies comparing proton therapy with other radiotherapy modalities. As a consequence, clinical studies assessing the benefits of proton therapy could potentially be biased in favour (or detriment) of proton therapy. Thus, a challenge for the radiation dosimetry of proton beams is to reduce the uncertainty associated to the determination of the absorbed dose to water and bring it down to the level of precision of high-energy photon beams. This thesis addresses this challenge.

1.2 State of the art

The large uncertainty (as compared to high-energy photon beams) associated to the determination of the absorbed dose to water in proton beams is mainly due to the uncertainty of the beam quality correction factors in proton beams (see section 2.2.4). At present, beam quality correction factors for proton beams are calculated theoretically as described in IAEA TRS-398. With this approach, the relative standard uncertainty of beam quality correction factors is $u = 1.6\%$ for cylindrical ionization chambers and $u = 2.1\%$ for plane-parallel ionization chambers—substantially larger than in high-energy photon beams ($u = 1.0\%$). In dealing with the expression of uncertainties, this work follows the recommendations of JCGM (2008).

Different attempts have been made to reduce the uncertainty of beam quality correction factors in proton beams. Some authors have determined them experimentally, using water calorimetry, for few ionization chamber models and proton beam qualities (Vatnitsky et al. 1996, Medin et al. 2006, Medin 2010). However, the number of experimental beam quality correction factors available in the literature is scarce and it does not fully satisfy the
needs of the proton therapy community. Other authors have used analytical models, Monte Carlo simulation methods (see section 2.3) and experimental measurements to calculate, or determine, some of the quantities involved in the theoretical calculation of beam quality correction factors, mainly ionization chamber-specific perturbation correction factors (Palmans & Verhaegen 1998, Palmans et al. 2001, Verhaegen & Palmans 2001, Palmans et al. 2002, Palmans 2006, 2011).

Sempau et al. (2004) proposed an alternative and more accurate approach to the calculation of beam quality correction factors, which is based on the detailed Monte Carlo simulation of ionization chambers (see section 2.2.4). Different authors have followed this novel approach to calculate the beam quality correction factors for high-energy photon beams (Wulff et al. 2008, González-Castaño et al. 2009, Muir & Rogers 2010, Muir et al. 2012, Erazo & Lallena 2013) and high-energy electron beams (Sempau et al. 2004, Zink & Wulff 2008, 2012, Muir & Rogers 2014, Erazo et al. 2014). However, this approach has never been used for proton beams. The reason for that is twofold. First, Monte Carlo simulation codes typically used in radiation dosimetry of radiotherapy beams, such as EGSnrc (Kawrakow 2000a) and Penelope (Baró et al. 1995, Sempau et al. 1997, Salvat 2014), which have been proven to accurately simulate the transport of radiation (especially low-energy electrons) in ionization chamber geometries (Kawrakow 2000b, Seuntjens et al. 2002, Sempau & Andreo 2006), do not include proton transport. Second, other Monte Carlo simulation codes commonly used in radiation therapy which do include proton transport—mainly Geant4 (Agostinelli et al. 2003), FLUKA (Ferrari et al. 2005, Battistoni et al. 2007) and MCNPX (Waters 2002)—have not yet been shown to achieve the level of accuracy needed for ionization chamber simulations (Poon et al. 2005, Elles et al. 2008, Klingebiel et al. 2011). As a consequence, no Monte Carlo calculations of beam quality correction factors in proton beams have been done so far using Sempau et al. (2004) approach.

1.3 Goals and structure

The main goal of this thesis is to improve the radiation dosimetry of clinical proton beams. That is, to improve the accuracy, reduce the uncertainty and propose a novel approach to the radiation dosimetry of proton pencil beams. The main focus is on the absolute determination of the absorbed dose to water in clinical proton pencil beams. However, this thesis also deals with relative dosimetry.

More in detail, the objectives of this work are:

1. To re-evaluate the water/air stopping-power ratios for proton pencil beams calculated by Medin & Andreo (1997). Water/air stopping-power ratio are a key quantity in both the relative and reference
dosimetry of proton beams.

2. To calculate water/medium stopping-power ratios for a range of detection materials typically used in the relative dosimetry of proton pencil beams.

3. To compare the reference dosimetry and Faraday cup dosimetry of proton pencil beams. The comparison of independent dosimetry techniques allows for the detection of potential systematic errors in the dosimetry process.

4. To experimentally validate the beam quality correction factors for proton beams tabulated in IAEA TRS-398. Beam quality correction factors are the cornerstone of the reference dosimetry of external radiotherapy beams. Such a validation contributes to reducing the uncertainty in the determination of the absorbed dose to water.

5. To calculate beam quality correction factors in proton beams using Monte Carlo simulation techniques. As mentioned above, Monte Carlo methods allow for a more accurate calculation of beam quality correction factors, which in turn contributes to improving the accuracy and reducing the uncertainty in the determination of the absorbed dose to water in proton pencil beams.

6. To suggest a novel approach to the reference dosimetry of proton pencil beams based on the concept of ‘dose-area product’.

This is a cumulative dissertation based on work that has already been published, is currently submitted for publication or will be submitted in the near future. The structure of this thesis is the following:

- Chapter 2 presents a brief summary of the physical interactions of protons with matter, together with a brief introduction to the fundamentals of radiation dosimetry and Monte Carlo simulation techniques applied to the transport of radiation in matter.

- Chapter 3 describes the calculation of water/medium stopping-power ratios for proton pencil beams.

- Chapter 4 presents a comparison between ionization chamber dosimetry based on IAEA TRS-398 and Faraday cup dosimetry—applied to the calibration of the beam monitor chamber in a proton pencil beam scanning delivery system.

- Chapter 5 reports on the experimental validation of beam quality correction factors for proton beams tabulated in IAEA TRS-398. It also describes the experimental determination of non-tabulated beam quality correction factors, based on the already existing values.
1.3. Goals and structure

- Chapter 6 describes the Monte Carlo calculation of beam quality correction factors for proton beams using the approach of Sempau et al. (2004).

- Chapter 7 presents a novel approach to the calibration of the beam monitor chambers in proton pencil beam scanning delivery systems based on the determination of the dose-area product of a single proton pencil beam.

- Finally, chapter 8 summarizes the main conclusions of this work and identifies the directions for future research in the field of radiation dosimetry of proton pencil beams.
2.1 Interactions of protons with matter

This section gives a brief summary of the interactions of protons with matter. As any charged particle, protons undergo electromagnetic interactions with the atoms of the medium. Also, when sufficiently energetic to penetrate the Coulomb barrier of the nucleus, protons do also interact with the nuclear potential.

In the energy range relevant to proton therapy (typically up to 250 MeV), the main interactions are:

- Elastic scattering with the atomic electrostatic potential
- Inelastic scattering with the atomic electrons
- Elastic and inelastic scattering with the nuclear potential

Elastic interactions are those in which the initial and final quantum states of the projectile and target atom are the same. That is, interactions in which, in the centre-of-mass (CM) frame, there is no energy transfer between the projectile and the target. On the contrary, inelastic interactions are those in which the initial and final quantum states of the target atom are different; i.e. interactions that involve an energy transfer between the projectile and the target in the CM frame. At the energy range relevant to proton therapy, bremsstrahlung emission has a negligible effect in the stopping of protons in matter and, therefore, it will not be discussed here.

In this section 2.1, the kinetic energy of a particle will be denoted by $T$ and its total energy (kinetic energy and rest mass) by $E$. Elsewhere in the document, $E$ refers to kinetic energy.

2.1.1 Electromagnetic interactions

Electromagnetic interactions refer to the interactions of protons with the electromagnetic potential of the atom.
Elastic scattering

This section is adapted from Salvat (2013). Protons interact elastically with the electromagnetic potential of the atom. In these elastic collisions, the kinetic energy of the proton is conserved in the CM frame, but its direction of propagation is modified. That is, in the CM frame, the energy transferred to the target atom \( W = E - E' \) is zero, but there is a momentum transfer, \( q \), given by

\[
q = |p - p'| = 2p \sin(\theta/2)
\]  

where \( p \) and \( p' \) are the initial and final linear momentum of the projectile, respectively, \( p \) is the magnitude of the momenta of the colliding particles, and \( \theta \) is the polar scattering angle.

In the field of proton therapy, the electromagnetic potential of the atom may be well described by the screened Coulomb potential

\[
V(r) = \frac{zZe^2}{r} \phi(r)
\]  

where \( z \) is the atomic number of the projectile \( (z = 1 \) for protons), \( Z \) is the atomic number of the target atom, \( e \) is the charge of the electron, \( r \) is the distance between the projectile and the nucleus (which is assumed to be a point charge) and \( \phi(r) \) is a function that accounts for the screening of the nuclear charge by the atomic electrons. \( \phi(r) \) equals to unity for \( r = 0 \), decreases monotonically with \( r \) and, for neutral atoms, tends to zero for \( r \to \infty \). Screening functions have multiple forms. Amongst the most popular are the Wentzel screening function

\[
\phi(r) = \exp\left(-\frac{r}{r_s}\right)
\]  

where \( r_s \) is the screening radius or screening length; or Molière’s parametrization of the Thomas-Fermi screening function (Molière 1947)

\[
\phi(r) = 0.10 \exp(-6r/r_s) + 0.55 \exp(-1.2r/r_s) + 0.35 \exp(-0.3r/r_s)
\]  

where \( r_s = (9\pi^2)^{1/3} 2^{2/3} Z^{-1/3} a_0 \) and \( a_0 \) is the Bohr radius, which is the basis of Molière’s multiple scattering theory (Molière 1948, Bethe 1953).

A simple approach to describe elastic collisions is provided by the Born approximation. It consists of approximating the wave functions of the projectile in the initial and final states by plane waves and treating the interaction potential as a first-order perturbation (Mott & Massey 1965). This approximation is valid for fast projectiles and light target atoms. The differential cross section for elastic scattering by a central potential obtained from the Born approximation is (Mott & Massey 1965)

\[
\frac{d\sigma}{d\Omega} = |j^B(\theta)|^2
\]
where $\theta$ is the polar scattering angle and

$$f^B(\theta) = -\frac{2\gamma m}{\hbar^2} \int \frac{\sin(qr/\hbar)}{qr/\hbar} V(r) r^2 \, dr$$  \hspace{1cm} (2.6)$$
is the Born scattering amplitude—where $\gamma$ is the Lorentz factor, $m$ is the mass of the projectile and $\hbar$ is the reduced Planck constant. For a central potential of the form of (2.2), with the Wentzel screening function (2.3), the Born scattering amplitude is

$$f^B(\theta) = -2\gamma m zZe^2 \left(\frac{c}{ch/\mathcal{r}_s}\right)^2 + \left(\frac{cq}{c}\right)^2$$  \hspace{1cm} (2.7)$$
and the differential cross section takes the form

$$\frac{d\sigma^B_{\text{el}}}{d\Omega} = \left(2\gamma mc^2 zZe^2\right)^2 \frac{1}{\left(\frac{c}{ch/\mathcal{r}_s}\right)^2 + \left(\frac{cq}{c}\right)^2}$$  \hspace{1cm} (2.8)$$
Note that for large momentum transfers the screening term becomes negligible and the Born differential cross section reduces to the Rutherford differential cross section

$$\frac{d\sigma^R_{\text{el}}}{d\Omega} = \left(2\gamma mc^2 Z^2e^2\right)^2 \frac{1}{\left(\frac{c}{cq}\right)^4}$$  \hspace{1cm} (2.9)$$
which is valid for large scattering angles. In the non-relativistic limit ($\gamma \to 1$), it reduces to

$$\frac{d\sigma^R_{\text{el}}}{d\Omega} = \left(\frac{Z^2e^2}{2mv^2}\right)^2 \frac{1}{\sin^4(\theta/2)}$$  \hspace{1cm} (2.10)$$
where $v$ is the velocity of the projectile.

More accurate descriptions of the elastic scattering with the electromagnetic potential of the atom, such as the Molière’s theory (Molière 1948, Bethe 1953) or the eikonal approximation proposed by Salvat (2013), can be found in the mentioned references.

As mentioned above, in the CM frame there is no energy transfer between the projectile and the target during the course of the interaction ($W_{\text{CM}}=0$), only momentum transfer (2.1). However, in the laboratory (L) frame, there is a transfer of kinetic energy from the projectile to the target atom ($W_L$). This energy transfer causes the projectile to lose part of its kinetic energy and the target atom to recoil after the elastic collision. The energy transfer in the L frame is determined by the scattering angle in the CM frame

$$W_L = \frac{p^2_{\text{CM}}}{M} (1 - \cos \theta_{\text{CM}})$$  \hspace{1cm} (2.11)$$
where $p_{\text{CM}}$ is the magnitude of the momenta of the colliding particles in the CM frame and $M$ is the rest mass of the target atom. Note that the energy
transfer is zero for $\theta_{cm} = 0$ (forward scattering) and reaches its maximum for $\theta_{cm} = \pi$ (back scattering)

$$W_{max} = \frac{2p_{cm}^2}{M}$$

(2.12)

In the non-relativistic limit, which is the scenario that applies to proton therapy, it may be approximated by

$$W_{max} = 4T \frac{mM}{(m + M)^2}$$

(2.13)

where $T$ is the kinetic energy of the projectile. Making use of equation (2.11), the differential cross section may be expressed in form of energy loss as

$$\left. \frac{d\sigma_{el}}{dW} \right|_L = \frac{2\pi}{\rho^2} \frac{d\sigma_{el}}{d\Omega} \left|_{CM} \right.$$ .

(2.14)

A quantity of interest in proton therapy is the nuclear stopping power, $S_{nuc}$, which is defined as the average energy loss per unit path length due to elastic collisions with the electromagnetic potential of the atom (Seltzer et al. 2011)

$$S_{nuc} \doteq N \int_0^{W_{max}} W \frac{d\sigma_{el}}{dW} dW$$

(2.15)

where $N$ is the number of target atoms (or molecules in compound materials) per unit volume. Note that the nuclear stopping power has nothing to do with the proton interactions with the nuclear potential, but with the elastic scattering with the electromagnetic potential of the screened nucleus. The nuclear stopping power is only important at very low energies. In water, its contribution to the total stopping power reaches the level of 1% only at kinetic energies below 20 keV (Berger et al. 1993), totally irrelevant to proton therapy.

Another quantity of interest is the so-called scattering power, $\Theta$, which is defined as the average angular deflection per unit path length due to elastic collisions (Salvat 2014)

$$\Theta \doteq 2N \int (1 - \cos \theta) \frac{d\sigma_{el}}{d\Omega} d\Omega = \frac{2}{\lambda} (1 - \langle \cos \theta \rangle)$$

(2.16)

where $\lambda = 1/N\sigma_{el}$ is the mean free path length between consecutive elastic interactions. Note that for small scattering angles ($\theta \ll 1$), $\Theta \approx (\theta^2) / \lambda$.

**Inelastic scattering**

This section is based on ICRU Report No. 49 (Berger et al. 1993). In addition to elastic interactions, protons also interact inelastically with the atomic electrons, leading to the excitation and ionization of the target atoms.
2.1. Interactions of protons with matter

Inelastic collisions are the dominant mechanism of energy loss for protons in matter.

One of the most important quantities in proton therapy is the electronic stopping power, $S_{el}$, which is defined as the average energy loss per unit path length due to inelastic collisions with the atomic electrons in the medium (Seltzer et al. 2011)

$$S_{el} = N \int_0^{W_{\text{max}}} W \frac{d\sigma_{\text{in}}}{dW} dW$$  \hspace{1cm} (2.17)

where $(d\sigma_{\text{in}}/dW)$ is the differential cross section for inelastic collisions. Note that here the terminology recommended by ICRU Report No. 85 (Seltzer et al. 2011), with the suffix ‘el’ for electronic, has nothing to do with elastic collisions.

The electronic stopping power of a charged particle may be expressed as

$$S_{el} = N \frac{4\pi z^2 Z e^4}{m_e v^2} L(\beta)$$  \hspace{1cm} (2.18)

where $N$ is the number of target atoms (or molecules in a compound material) per unit volume, $z$ is the atomic number of the projectile, $Z$ is the atomic number of the target atom, $e$ is the charge of the electron, $m_e$ is the rest mass of the electron, $v$ is the velocity of the projectile and $L(\beta)$ is a quantity called stopping number, which is typically expressed in terms of the projectile velocity in units of the speed of light ($\beta = v/c$). The quantities preceding the stopping number take into account the gross features of the energy-loss process, whereas $L$ takes into account the fine details. Note that, the electronic stopping power (2.18) is inversely proportional to $v^2$. That is, the slower the projectile, the more energy is transferred to the medium. This behaviour explains, in part, the characteristic shape of proton (and charged-particles heavier than protons) energy deposition in depth, the so-called Bragg peak—see figure 2.1(a).

In the Bethe formulation of the electronic stopping power, the stopping number may be expressed as (Berger et al. 1993)

$$L_0(\beta) = \frac{1}{2} \ln \left( \frac{2m_e c^2 \beta^2 W_{\text{max}}}{1 - \beta^2} \right) - \beta^2 - \ln I - \frac{C}{Z} - \frac{\delta}{2}$$  \hspace{1cm} (2.19)

where $I$ is the mean excitation energy of the medium, $C/Z$ is the shell correction and $\delta/2$ is the density effect correction. $W_{\text{max}}$ is the largest possible energy loss in a single collision with a free electron, and it is given by

$$W_{\text{max}} = \frac{2m_e c^2 \beta^2}{1 - \beta^2} \left[ 1 + 2\gamma \frac{m_e}{m} + \left( \frac{m_e}{m} \right)^2 \right]^{-1}$$  \hspace{1cm} (2.20)

where $m$ is the mass of the projectile. Do not mix up with equation (2.12), which applies to elastic collisions. In the high-energy limit ($\gamma \to \infty$), $W_{\text{max}}$
approaches to the kinetic energy of the projectile, regardless of its mass. In the non-relativistic limit ($\gamma \to 1$), which is the scenario that applies to proton therapy,

$$W_{\text{max}} \approx 2m_e v^2 = 4 \left( \frac{m_e}{m} \right) T.$$  \hspace{1cm} (2.21)

In the case of protons ($m_p \approx 1836 m_e$), $W_{\text{max}} \sim E/450$.

The Bethe formulation of the stopping-power (Bethe 1930) was derived on the basis of the first-order Born approximation—i.e. it is valid for projectiles with large velocities, as compared to the velocity of the atomic electrons. As the velocity of the projectile decreases, the cross sections for inelastic scattering with the electrons in the deepest shells (K-shell, L-shells, etc.) start to vanish. The shell correction term ($C/Z$) in equation (2.19) takes this effect into account. In the case of protons in water, the contribution of the shell correction to $L$ reaches the level of 1% only for $T < 10$ MeV (Andreo et al. 2013). Finally, the density effect correction term ($\delta/2$) takes into account that the passage of a projectile polarizes the medium and this polarization results in a reduction of the stopping-power. Unlike the shell correction, the density effect correction is only relevant at high-energies ($T \geq mc^2$). For instance, in the case of protons in water, its contribution to $L$ reaches the level of 1% only for $T > 1$ GeV (Andreo et al. 2013).

Furthermore, two more terms are typically added to the Bethe formulation of the stopping number (2.19): the Barkas correction ($zL_1$) and the Bloch correction ($z^2 L_2$) (Berger et al. 1993)

$$L(\beta) = L_0(\beta) + z L_1(\beta) + z^2 L_2(\beta)$$  \hspace{1cm} (2.22)

These terms take into account additional departures from the first-order Born approximation and are important only for low projectile velocities. For example, in the case of protons in water, their contribution to $L$ reaches the level of 1% only for $T < 3$ MeV (Andreo et al. 2013).

### 2.1.2 Nuclear interactions

Nuclear interactions refer to the interactions of protons with the nuclear potential. Unlike electromagnetic interactions, in which the interaction potential is known, nuclear forces are only described approximately. Evaluated nuclear cross sections are based on a combination of experimental data and theoretical models optimized to reproduce the experiments (Chadwick et al. 2000). Thus, in this section, proton nuclear interactions will only be described qualitatively.

As electromagnetic interactions, nuclear interactions may also be classified in elastic and inelastic collisions. In this case, inelastic nuclear interactions not only lead to the excitation of target nuclei, but also to nuclear fragmentation and particle transfer reactions.
In the field of proton therapy, the effect of elastic nuclear interactions—or inelastic nuclear interactions leading to a mild excitation of target nuclei—is, in general, very similar to the effect of electromagnetic interactions, i.e. they lead to a small energy loss and angular deflection of the proton projectile. The exception are elastic nuclear interactions with the hydrogen nuclei in the medium. In this particular case, the two outgoing protons (the incident proton and the target hydrogen nucleus) share the kinetic energy of the projectile and they may exit the collision with large scattering angles (Gottschalk 2012).

On the contrary, inelastic nuclear interactions produce a very different effect than electromagnetic interactions: they “remove” protons from the beam and they deposit part of their energy outside the beam path. In proton therapy argot, primary protons refer to those protons that have suffered electromagnetic interactions only; whereas secondary protons typically refer to those protons resulting from inelastic nuclear interactions. More in detail, inelastic nuclear interactions produce the following types of secondary particles:

(i) Secondary protons. These are typically low-energy protons with large scattering angles. They deposit their energy up to few centimetres away from the interaction point.

(ii) Neutral particles (photons and neutrons). Typically these particles deposit their energy far from the primary beam path.

(iii) Charged particles heavier than protons (mainly $^2\text{H}$, $^3\text{H}$ and $\alpha$-particles) and recoil nuclei. These particles have very short ranges and, therefore, they deposit their energy in the vicinity of the interaction point. Secondary particles heavier than $\alpha$-particles are rare—see for instance figure 3.2.

In the energy range relevant to proton therapy, total cross sections for inelastic nuclear scattering are nearly constant with energy, except at low energies where they increase before falling to zero (Chadwick et al. 2000, Gottschalk 2012). This increase in the total cross sections for inelastic nuclear scattering with decreasing energy is similar to the increase in the total cross section for inelastic electromagnetic scattering—which makes the probability of inelastic nuclear interaction, with respect to other interaction mechanisms, nearly constant with proton energy.

In proton therapy we are sometimes interested in assessing the probability of a proton suffering an inelastic nuclear interaction at some point of its track and being therefore “removed” from the primary beam. As mentioned above, the total cross section for inelastic nuclear scattering is approximately constant with energy. On a first approximation, the probability of a proton suffering an inelastic nuclear interaction per unit path length may also
be considered nearly constant—as a rule of thumb, this probability is commonly taken as 1% per cm. Thus, the higher the initial kinetic energy of the proton beam, the longer the range of the protons and, therefore, the higher the percentage of protons suffering an inelastic nuclear interaction at some point of their track and being removed from the primary beam. At the very end of range, i.e. in the Bragg peak region, the probability of inelastic nuclear interaction falls to zero at the same time that the probability of inelastic electromagnetic interaction increases drastically—see equation (2.18).
2.2 Fundamentals of radiation dosimetry

This section describes, in brief, the fundamental quantities, theories and protocols that form the basis of current radiation dosimetry of clinical proton beams.

2.2.1 Fundamental quantities

This section is based on ICRU Report No. 85 (Seltzer et al. 2011). It summarizes only those quantities relevant to the radiation dosimetry of clinical proton beams.

**Fluence**

Let \( N \) be the expectation value of the number of particles incident on a sphere of cross-sectional area \( d\alpha \). Then the fluence, \( \Phi \), is defined as

\[
\Phi = \frac{dN}{d\alpha}
\]  

(2.23)

and its units are m\(^{-2}\). The use of a sphere of cross-sectional area \( d\alpha \) expresses the fact that, in the definition of fluence, one considers an area \( d\alpha \) always perpendicular to the direction of each particle.

An alternative, and equivalent, definition of fluence is

\[
\Phi = \frac{dl}{dV}
\]

(2.24)

where \( dl \) is (the expectation value of) the sum of all the particle track lengths in an infinitesimal volume \( dV \).

**Energy imparted**

The energy imparted, \( \epsilon \), in a given volume is defined as

\[
\epsilon = \epsilon_{\text{in}} - \epsilon_{\text{out}} + Q
\]

(2.25)

where \( \epsilon_{\text{in}} \) is the sum of the kinetic energy of all the ionizing particles entering the volume, \( \epsilon_{\text{out}} \) is the sum of the kinetic energy of all the ionizing particles exiting the volume, and \( Q \) is the conversion of rest mass in kinetic energy in the volume (\( Q > 0 \): rest mass converted to kinetic energy; \( Q < 0 \): kinetic energy converted to rest mass).

**Absorbed dose**

The absorbed dose, \( D \), is a point quantity defined from a stochastic quantity, \( \epsilon \). It is defined as the expected value of the energy imparted, \( d\epsilon \), in a volume \( dV \) of mass \( dm \)

\[
D = \frac{d\epsilon}{dm}
\]

(2.26)
i.e. is the expected value of the energy imparted per unit mass. Its unit is the gray, Gy = J kg\(^{-1}\).

**Stopping power**

The *stopping power*, \(S\), also called *linear stopping power*, is a quantity defined for charged particles only. As mentioned above in section 2.1.1, it is defined as the average kinetic energy loss per unit path length, in a given material. Alternatively to equations (2.15) and (2.17), it may also be expressed macroscopically as

\[ S = \frac{dE}{dl} \]  

with units of J m\(^{-1}\) or, more commonly, MeV cm\(^{-1}\). The total stopping power, \(S\), may also be expressed as the sum of its independent components:

\[ S = S_{el} + S_{rad} + S_{nuc} \]

where \(S_{el}\) is the *electronic stopping power* due to inelastic electromagnetic interactions with the atomic electrons (2.17), \(S_{rad}\) is the *radiative stopping power* due to bremsstrahlung emission in the electric fields of the atomic nuclei and electrons, and \(S_{nuc}\) is the *nuclear stopping power* due to elastic electromagnetic interactions with the atomic nuclei (2.15). Note that, in the frame of clinical proton therapy, the relevant quantity is \(S_{el}\).

More commonly used in radiation dosimetry is the *mass stopping power*, which is defined as the ratio between the stopping power and the material mass density, \(S/\rho\).

**Linear energy transfer**

The *linear energy transfer* or *restricted linear electronic stopping power*, \(L_\Delta\), of a given charged particle in a given material is defined as

\[ L_\Delta = \frac{dE_\Delta}{dl} \]  

where \(dE_\Delta\) is the average energy loss by the charged particle in inelastic electromagnetic collisions with the atomic electrons, minus the sum of the kinetic energy of all secondary electrons with kinetic energy \(E > \Delta\). Its units are J m\(^{-1}\) (or more commonly MeV cm\(^{-1}\)). This definition expresses the following energy balance: energy lost by the primary charged particle in inelastic electromagnetic interactions with the atomic electrons, minus the energy carried away by energetic secondary electrons with initial kinetic energy \(E > \Delta\), equals to energy “deposited locally”. That is, while \(S_{el}\) describes the energy ‘lost’ by the charged particle, \(L_\Delta\) describes the energy ‘deposited locally’ (i.e. in the vicinity of the interaction point) by the charged particle. Note that \(L_\Delta\) includes the binding energy of atomic electrons for all interactions. As a consequence, \(L_0\) refers to the energy loss (per unit path length) due to inelastic electromagnetic interactions that lead to atomic excitations only (no ionization), whereas \(L_\infty = S_{el}\).
2.2. Fundamentals of radiation dosimetry

CSDA Range

The Continuous Sloowing Down Approximation, CSDA, assumes that charged particles lose their energy continuously, at a pace determined by the (total) stopping power. That is, the CSDA does not take into account the stochastic character of the interactions of charged particles with matter, so that the predicted range for all primary particles is identical. Thus, in the continuous slowing down approximation, the range, $R_{\text{CSDA}}$, of a charged particle is

$$R_{\text{CSDA}} = \int_{0}^{l_{\text{max}}} dl = \int_{0}^{E_{0}} \frac{dE}{S(E)}$$

(2.29)

where $E_{0}$ is the initial kinetic energy of the charged particle.

In proton beams, $R_{\text{CSDA}}$ can in good approximation be determined experimentally as $R_{80}$ (Bortfeld 1997), where $R_{80}$ is the depth at which the absorbed dose beyond the Bragg peak (see figure 2.1(a)) falls to 80% of its maximum value.

2.2.2 Cavity theory

This section is based on Attix (1986).

Absorbed dose in thin foils

Before presenting the different cavity theories, this section describes the calculation of the absorbed dose in thin foils. Let us consider a parallel beam of charged particles of kinetic energy $E_{0}$ impinging perpendicularly on a foil of material $m$. Let us assume that:

1. $S_{\text{el}}$ is the dominant contribution to the total stopping power, so that $S \simeq S_{\text{el}}$.

2. The foil is thin enough so that $S_{\text{el}}$ remains constant and characteristic of $E_{0}$.

3. The foil is thin enough so that the trajectories of the particles are straight, i.e. scattering is negligible.

4. The net kinetic energy carried away by secondary electrons is negligible, either because the foil is thick compared to the range of secondary electrons, or because the foil is sandwiched between two identical foils that provide charged particle equilibrium for secondary electrons.

5. Bremsstrahlung photons escape the foil without interacting.

Under these assumptions, the absorbed dose in the foil of material $m$ is

$$D_{m} = \Phi \cdot \left( \frac{S_{\text{el}}(E_{0})}{\rho} \right)_{m}$$

(2.30)
where $\Phi$ is the fluence of charged particles in the foil and $(S_{el}(E_0)/\rho)_m$ is the mass electronic stopping power of the charged particle in the material $m$, evaluated at $E_0$.

If the incident beam is polyenergetic, the absorbed dose in the foil is

$$D_m = \int_0^{E_{\text{max}}} \Phi(E) \left( \frac{S_{el}(E)}{\rho} \right)_m \, dE \quad (2.31)$$

where $\Phi(E)$ is the distribution of fluence with respect to the energy of charged particles in the foil.

### Bragg–Gray theory

Cavity theories study the relationship between the absorbed dose in a homogeneous cavity inside a homogeneous medium, $D_{\text{cav}}$, and the absorbed dose at a point in the medium in the absence of the cavity, $D_m$.

In particular, the Bragg–Gray theory is based on the following two assumptions:

1. The size of the cavity is small compared to the range of the charged particles that cross it, so that the cavity does not perturb the fluence of charged particles in the medium.

2. The absorbed dose in the cavity is deposited only by the charged particles that cross it.

If these two assumptions (also called Bragg–Gray conditions) are fulfilled, the ratio between the absorbed dose in the medium and the absorbed dose in the cavity is

$$\frac{D_m}{D_{\text{cav}}} = \frac{\int_0^{E_{\text{max}}} \Phi_m(E) \left( \frac{S_{el}(E)}{\rho} \right)_m \, dE}{\int_0^{E_{\text{max}}} \Phi_m(E) \left( \frac{S_{el}(E)}{\rho} \right)_{\text{cav}} \, dE} \equiv s_{\text{BG}} \quad (2.32)$$

where $\Phi_m(E)$ is the distribution of fluence with respect to the energy of primary charged particles in the medium and $S_{el}$ is the electronic stopping power. The last equality defines the Bragg–Gray medium/cavity stopping-power ratio, $s_{\text{BG},\text{cav}}$.

Note that Bragg–Gray theory is based on equation (2.31) and, therefore, it is also based on the underlying assumptions described in the previous section. In particular, it assumes that secondary electrons deposit their energy locally or the existence of charged particle equilibrium for secondary electrons.

### Spencer–Attix theory

The Spencer–Attix cavity theory is a refinement of the Bragg–Gray theory. Although it keeps on assuming that the cavity does not perturb the fluence
of charged particles in the medium, it takes into account that secondary electrons do not deposit all their energy locally.

The Spencer–Attix theory was initially derived assuming that the only charged particles that contributed significantly to the absorbed dose in the medium were electrons. In this context, it introduces the parameter $\Delta$, which is defined as the mean energy of the electrons with a sufficient range to cross the cavity. Based on this parameter, a distinction is made between secondary electrons with kinetic energy $E < \Delta$ (i.e. with sufficient energy to cross and leave the cavity), which deposit part of their kinetic energy outside the cavity.

According to Spencer–Attix cavity theory, the ratio between the absorbed dose in the medium and the absorbed dose in the cavity is

$$\frac{D_m}{D_{cav}} = \int_{E_{\text{max}}}^{E_{\text{cut}}} \Phi_m(E) \left( \frac{L_\Delta(E)}/\rho \right)_m dE + \Phi_m(\Delta) \left( \frac{S_{\text{el}}(\Delta)}/\rho \right)_m \Delta = s_{\text{SA},m,cav}$$

(2.33)

where $\Phi_m(E)$ is the distribution of fluence with respect to the energy of all electrons (primary and secondary) in the medium, $L_\Delta$ is the linear energy transfer (2.28), and $S_{\text{el}}$ is the electronic stopping power. The last term of the sum, $\Phi(\Delta) \left( \frac{S_{\text{el}}(\Delta)}/\rho \right) \Delta$, is the so-called track-end contribution (Nahum 1978), where $\Phi(\Delta)$ is the fluence evaluated at $E = \Delta$ (not the distribution of fluence with respect to $\Delta$). The last equality defines the Spencer–Attix medium/cavity stopping-power ratio, $s_{\text{SA},m,cav}$.

When not only electrons, but also other charged particles, contribute to the absorbed dose in the cavity, the above formulation of the Spencer–Attix theory (2.33) may be generalised as follows

$$s_{\text{SA},m,cav} = \sum_i \int_{E_{\text{cut}}}^{E_{\text{max}}} \Phi_m^i(E) \left( \frac{L_\Delta(E)/\rho}{\rho} \right)_m dE + \Phi_m^i(E_{\text{cut}}) \left( \frac{S_{\text{el}}(E_{\text{cut}})/\rho}{\rho} \right)_m E_{\text{cut}}^i$$

(2.34)

where $i$ are the different types of charged particles that contribute to the absorbed dose in the cavity; $E_{\text{cut}}^i$ is defined as the mean energy of the $i$-th particle type with a sufficient range to cross the cavity (for electrons, $E_{\text{cut}} = \Delta$); $\Phi_m^i(E)$ is the distribution of the fluence with respect to the energy of the $i$-th particle type in the medium; and $(L_\Delta/\rho)_m^i$ and $(S_{\text{el}}/\rho)_m^i$ are the mass linear energy transfer and the mass electronic stopping power, respectively, of the $i$-th particle type.

Let us analyse equation (2.34) in more detail. The first term of the sum, $\int_{E_{\text{cut}}}^{E_{\text{max}}} \Phi(E) \left( \frac{L_\Delta(E)/\rho}{\rho} \right) dE$, is the contribution of charged particles with kinetic energy $E > E_{\text{cut}}$. These charged particles lose part of their energy due to inelastic electromagnetic collisions with the atomic electrons, giving
rise to secondary electrons. Note that \( L_\Delta \) implies that only those secondary electrons with kinetic energy \( E < \Delta \) contribute to the absorbed dose at that point. The second term of the sum is the contribution of the track-ends. Track-ends are charged particles with kinetic energy \( E < E_{\text{cut}} \), whose track ends in the cavity and, therefore, they deposit all their energy in the cavity.

The final expression of the track-end contribution is derived as follows. A priori, the track-end contributions, in what follows abbreviated as TE, for a given charged particle type should be

\[
TE = \int_0^{E_{\text{cut}}} \Phi(E) \left( \frac{L_\Delta(E)}{\rho} \right) dE
\]  

(2.35)

By definition, track-ends deposit all their energy in the cavity. Thus, \( L_\Delta(E) = S_{\text{el}}(E) \). Additionally, in the continuous slowing down approximation, it can be shown that, for a given energy, the fluence of primary charged particles \( \Phi(E) \) is inversely proportional to the stopping power \( S(E) \) (Sempau 2006). Thus, it satisfies that

\[
\Phi(E) = \Phi(E_{\text{cut}}) \frac{S_{\text{el}}(E_{\text{cut}})}{S_{\text{el}}(E)}
\]  

(2.36)

Hence, substituting in equation (2.35),

\[
TE = \int_0^{E_{\text{cut}}} \Phi(E_{\text{cut}}) \frac{S_{\text{el}}(E_{\text{cut}})}{S_{\text{el}}(E)} \left( \frac{S_{\text{el}}(E)}{\rho} \right) dE = \Phi(E_{\text{cut}}) \left( \frac{S_{\text{el}}(E_{\text{cut}})}{\rho} \right) E_{\text{cut}}
\]  

(2.37)

### 2.2.3 Ionization chambers

Air-filled ionization chambers are the reference detectors in the dosimetry of radiotherapy beams. They allow to determine the absorbed dose in the medium (typically water) from the direct measurement of the ionization produced in the cavity.

#### Perturbation factors

The determination of the absorbed dose in the medium with an ionization chamber is based on the cavity theory. However, real ionization chambers do not fulfil Bragg–Gray conditions with the level of accuracy needed in radiation therapy. In particular, they do not fulfil the requirement that the cavity should not perturb the fluence of charged-particles in the medium. For the particular case of clinical proton beams, one could assume that, on a first approximation, this requirement is fulfilled by protons (as they undergo little scattering); but not by the secondary electrons resulting from inelastic electromagnetic interactions.
Thus, in order to keep on using the cavity theory formalism, the concept of perturbation correction factor or simply perturbation factor, $p$, is introduced, so that the relationship between the absorbed dose in the medium and the absorbed dose in the cavity is expressed as

$$D_m = D_{cav} \cdot s_{m,cav} \cdot p$$  \hspace{1cm} (2.38)

Historically, the global perturbation factor of a given detector, $p$, has been assumed to be the product of different and independent perturbation factors, $p_i$, i.e. $p = \prod p_i$. Typical perturbation factors of ionization chambers used in the dosimetry of external radiotherapy beams are $p_{cav}$, $p_{cel}$, $p_{dis}$ and $p_{wall}$, which take into account that the cavity, the central electrode and the wall of the ionization chamber are not equivalent to the medium, typically water——see Andreo et al. (2000) for a detailed definition of these terms.

The assumption of independent perturbation factors is, nevertheless, debatable. When the fluence of charged particles in both the medium and the cavity is known, it is possible to calculate the global perturbation factor of a detector, avoiding the unnecessary assumption of different independent perturbation factors (Nahum 1996). From equation (2.38), and using the generalised Spencer–Attix theory (2.34), it follows that the global perturbation factor of a given detector is

$$p = \frac{\sum_i \int_{E_{cut}}^{E_{max}} \Phi_i^m(E) \left( L(E)/\rho \right)_{cav}^i \, dE + \Phi_i^m(E_{cut}) \left( S_{cel}(E_{cut})/\rho \right)_{cav}^i E_{cut}^i \, dE}{\sum_i \int_{E_{cut}}^{E_{max}} \Phi_i^{cav}(E) \left( L(E)/\rho \right)_{cav}^i E_{cut}^i \, dE + \Phi_i^{cav}(E_{cut}) \left( S_{cel}(E_{cut})/\rho \right)_{cav}^i E_{cut}^i}$$  \hspace{1cm} (2.39)

where $i$ are the different types of charged particles that contribute to the absorbed dose in the cavity.

Finally, if the fluence of charged particles in both the medium and the detector cavity is known, it is also unnecessary to split the proportionality between $D_m$ and $D_{cav}$ in two factors: $s_{m,cav}$ and $p$. That is, the relationship between the absorbed dose in the medium and the absorbed dose in the cavity may also be expressed as (Sempau et al. 2004)

$$D_m = D_{cav} \cdot f$$  \hspace{1cm} (2.40)

where, using the generalised Spencer–Attix theory (2.34), it follows that

$$f = \frac{\sum_i \int_{E_{cut}}^{E_{max}} \Phi_i^m(E) \left( L(E)/\rho \right)_{m}^i \, dE + \Phi_i^m(E_{cut}) \left( S_{cel}(E_{cut})/\rho \right)_{m}^i E_{cut}^i \, dE}{\sum_i \int_{E_{cut}}^{E_{max}} \Phi_i^{cav}(E) \left( L(E)/\rho \right)_{cav}^i \, dE + \Phi_i^{cav}(E_{cut}) \left( S_{cel}(E_{cut})/\rho \right)_{cav}^i E_{cut}^i}$$  \hspace{1cm} (2.41)

where, again, $i$ extends over the different types of the charged particles that contribute to the absorbed dose in the medium and the cavity.
Absorbed dose in the ionization chamber cavity

Ionization chambers collect the electric charge, \( Q \), produced in the ionization chamber cavity as a consequence of the ionization of the cavity medium, typically air. Theoretically speaking, the absorbed dose in air, \( D_{\text{air}} \), in the ionization chamber cavity could be determined from the collected electric charge (assuming that all produced charge is collected) as follows

\[
D_{\text{air}} = \frac{Q}{v \rho_{\text{air}}} \frac{W_{\text{air}}}{e}
\]

(2.42)

where \( v \) is the sensitive volume of the ionization chamber, \( \rho_{\text{air}} \) is the density of air, \( e \) is the charge of the electron and \( W_{\text{air}} \) is the mean energy needed to create an ion pair in air.

In practice, however, the sensitive volume of the ionization chambers typically used in the dosimetry of radiotherapy beams is not known with sufficient accuracy. Thus, in order to determine the absorbed dose to air, or directly to water, with sufficient accuracy, one has to resort to the calibration of ionization chambers. This point is addressed in the following section.

2.2.4 IAEA TRS-398 Code of Practice

The IAEA TRS-398 Code of Practice is an international consensus document that issues recommendations for the determination of the absorbed dose to water in external radiotherapy beams. This section of the thesis covers all the points relevant to clinical proton beams, i.e. the formalism based on standards of absorbed dose to water, the quality index for proton beams and the reference conditions for the determination of the absorbed dose to water in proton beams. It is based on Andreo et al. (2000).

\( N_{D,w} \) based formalism

The absorbed dose to water in a beam quality \( Q \), \( D_{w,Q} \), in the absence of the ionization chamber, is given by

\[
D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0}
\]

(2.43)

where \( M_Q \) is the reading of the ionization chamber corrected for all the quantities of influence (except for the beam quality), \( N_{D,w,Q_0} \) is the calibration coefficient of the ionization chamber in terms of absorbed dose to water in the reference beam quality \( Q_0 \), and \( k_{Q,Q_0} \) is the beam quality correction factor. \( k_{Q,Q_0} \) corrects for the different response of the ionization chamber in the user beam quality \( Q \) and the calibration beam quality \( Q_0 \). The determination of the absorbed dose to water in a user beam quality \( Q \) with an ionization chamber calibrated in a reference beam quality \( Q_0 \) that might be different from the user beam quality is commonly called "reference dosimetry."
The raw reading of the ionization chamber should be corrected for all the quantities that influence the quantity under measurement—in this case, the collected charge—using appropriate correction factors, \( k_i \). These influence quantities, and their corresponding correction factors, are: pressure and temperature of the chamber air \((k_{TP})\), humidity of air \((k_h)\), electrometer calibration \((k_{elec})\), voltage polarity \((k_{pol})\) and ion recombination \((k_s)\). These factors are described in detail in Andreo et al. (2000).

The calibration coefficient in terms of absorbed dose to water in the reference beam quality \( Q_0 \) is given by

\[
N_{D,w,Q_0} = \frac{D_{w,Q_0}}{M_{Q_0}}
\]  

(2.44)

where \( D_{w,Q_0} \) is the absorbed dose to water at the reference measurement point in the reference beam quality \( Q_0 \) under reference conditions, and \( M_{Q_0} \) is the reading of the ionization chamber corrected for all the influence quantities mentioned above. Typically, the reference beam quality is \(^{60}\text{Co} \) gamma radiation.

**Beam quality correction factor**

As mentioned above, the beam quality correction factor, \( k_{Q,Q_0} \), corrects for the different response of the ionization chamber in the user beam quality \( Q \) and the calibration beam quality \( Q_0 \). It is defined as the ratio of the ionization chamber calibration coefficients (in terms of absorbed dose to water) at the beam qualities \( Q \) and \( Q_0 \)

\[
k_{Q,Q_0} = \frac{N_{D,w,Q}}{N_{D,w,Q_0}} = \frac{D_{w,Q}/M_Q}{D_{w,Q_0}/M_{Q_0}}
\]  

(2.45)

Ideally, beam quality correction factors should be determined experimentally in a Primary Standards Dosimetry Laboratory (PSDL) with a beam quality-independent metrology primary standard, such as a water calorimeter. However, such an experimental determination is seldom possible in PSDLs, mainly because of the difficulty in reproducing the user beam quality. This is certainly the case for proton beams, since at present no PSDL is equipped with proton beam qualities. When experimental beam quality correction factors are not available, they can also be calculated theoretically as (Andreo 1992)

\[
k_{Q,Q_0} = \frac{s_{w,air,Q}}{s_{w,air,Q_0}} \frac{W_{air,Q}}{W_{air,Q_0}} \frac{p_Q}{p_{Q_0}}
\]  

(2.46)

where \( s_{w,air} \) is the Spencer–Attix water/air stopping-power ratio (defined in section 2.2.2), \( W_{air} \) is the mean energy needed to create an ion pair in air (defined in section 2.2.3) and \( p \) is the perturbation correction factor of the ionization chamber (also defined in section 2.2.3).
Finally, and this is not included in IAEA TRS-398, Sempau et al. (2004) proposed an alternative and more accurate approach to the calculation of beam quality correction factors, which exploits the potential of Monte Carlo simulation techniques. From the principles of cavity theory (see section 2.2.2), it follows from equation (2.46) that beam quality correction factors can also be calculated as

\[
k_{Q,Q_0} = \frac{f_Q \ W_{\text{air},Q_0}}{f_{Q_0} \ W_{\text{air},Q_0}} = \frac{(D_w/D_{\text{air}})_Q}{(D_w/D_{\text{air}})_0} \ W_{\text{air},Q} \ W_{\text{air},Q_0}
\]

(2.47)

where \( f \) is an ionization chamber-specific and beam quality-dependent factor, defined above in equation (2.40), that establishes the proportionality between the absorbed dose to water at the reference point of measurement in the absence of the detector (\( D_w \)) and the average absorbed dose to air in the ionization chamber sensitive volume (\( D_{\text{air}} \)).

Due to a lack of experimental data and Monte Carlo calculated data at the time of publication, IAEA TRS-398 uses equation (2.46) to calculate the beam quality correction factors for clinical proton beams. \(^{60}\text{Co} \) gamma radiation is taken as reference beam quality. In this case, the subscript \( Q_0 \) in \( k_{Q,Q_0} \) is typically omitted. In what follows, we will adopt this nomenclature. The values entering in equation (2.46) are the following:

- For \(^{60}\text{Co} \) gamma radiation, IAEA TRS-398 adopts the water/air stopping-power ratio value of \( s_{w,\text{air},Q_0} = 1.133 \) (Andreo et al. 1986) and \( W_{\text{air},Q_0} = 33.97 \text{ eV} \). The perturbation correction factors are ionization chamber-specific and are tabulated for a wide range of cylindrical and plane-parallel ionization chambers.

- For proton beams, IAEA TRS-398 adopts the water/air stopping-power ratios calculated by Medin & Andreo (1997) for monoenergetic proton beams and \( W_{\text{air},Q} = 34.23 \text{ eV} \). Due to a lack of experimental and Monte Carlo data, perturbation correction factors are taken to be unity.

All the values entering into equation (2.46) are associated with an estimated uncertainty. Table 2.1 shows the estimates of the relative standard uncertainty of all the values entering into the IAEA TRS-398 calculation of \( k_Q \) factors for proton beams, as well as the combined standard uncertainty of the \( k_Q \) factors themselves.

**Beam quality index**

At the time of IAEA TRS-398 publication, the vast majority of proton therapy treatments were delivered with modulated proton beams, which generate the so-called *spread-out Bragg peak* (SOBP) fields—see figure 2.1(b).
2.2. Fundamentals of radiation dosimetry

Figure 2.1: (a) Depth-dose curve of a quasi-monoenergetic proton beam, commonly called Bragg peak. (b) Depth-dose curve of a modulated proton beam (red solid line), commonly called spread-out Bragg peak (SOBP); and depth-dose curves of the individual Bragg peaks that form the SOBP (blue solid lines).
Table 2.1: Estimated relative standard uncertainty of all the components entering into the calculation of $k_Q$ and combined relative standard uncertainty of the $k_Q$ factors for proton beams. All values are in %. A distinction is made between cylindrical and plane-parallel ionization chambers. Adapted from Andreo et al. (2000).

<table>
<thead>
<tr>
<th></th>
<th>Cylindrical</th>
<th>Plane-parallel</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{60}\text{Co }\gamma$-rays</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$s_{w,\text{air}}$</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Assignment $s_{w,\text{air}}$ to $Q_0$</td>
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</tr>
<tr>
<td>$W_{\text{air}}$</td>
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<td></td>
</tr>
<tr>
<td>$pQ_0$</td>
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<td>1.5</td>
</tr>
<tr>
<td>Protons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$s_{w,\text{air}}$</td>
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<tr>
<td>$k_Q$</td>
<td>1.6</td>
<td>2.1</td>
</tr>
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</table>

spread-out Bragg peak is the superposition of quasi-monoenergetic proton beams of different energy and intensity so that it creates a region of uniform dose in depth. The beam quality index for proton beams is the so-called residual range, $R_{\text{res}}$. At the measurement depth $z$ the residual range is defined as

$$R_{\text{res}} = R_p - z$$

where $R_p$ is the practical range, which is defined as the depth at which the absorbed dose beyond the Bragg peak or SOBP falls to 10% of its maximum value. Note that, based on this definition, the beam quality $Q$ is not unique for a particular proton beam, but it is also determined by the measurement depth.

Reference conditions for the determination of the absorbed dose to water

Table 2.2 summarizes the reference conditions for the determination of the absorbed dose to water in proton beams recommended by IAEA TRS-398. Note, from the recommendation on the measurement depth, that these conditions were mainly thought for modulated proton beams. However, the footnote in table 2.2 opens the door also to monoenergetic, or quasi-monoenergetic, proton beams. The terms quasi-monoenergetic or pseudo-monoenergetic will be used indistinctively in this work to stress that clinical proton beams are not monoenergetic, but they have an inherent initial energy spread.
Table 2.2: IAEA TRS-398 reference conditions for the determination of the absorbed dose to water in proton beams. Taken from Andreo et al. (2000).

<table>
<thead>
<tr>
<th>Influence quantity</th>
<th>Reference value or reference characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phantom material</td>
<td>Water</td>
</tr>
<tr>
<td>Chamber type</td>
<td>For $R_{\text{res}} \geq 0.5 \text{ g cm}^{-2}$, cylindrical and plane-parallel</td>
</tr>
<tr>
<td></td>
<td>For $R_{\text{res}} &lt; 0.5 \text{ g cm}^{-2}$, plane-parallel</td>
</tr>
<tr>
<td>Measurement depth $z_{\text{ref}}$</td>
<td>Middle of the SOBP†</td>
</tr>
<tr>
<td>Reference point of the chamber</td>
<td>For plane-parallel chambers, on the inner surface of the window at its centre</td>
</tr>
<tr>
<td></td>
<td>For cylindrical chambers, on the central axis at the centre of the cavity volume</td>
</tr>
<tr>
<td>Position of the reference point of the chamber</td>
<td>At the point of measurement depth $z_{\text{ref}}$</td>
</tr>
<tr>
<td>Source-surface distance</td>
<td>Clinical treatment distance</td>
</tr>
<tr>
<td>Field size at the phantom surface</td>
<td>10 cm $\times$ 10 cm, or that used for normalisation of the output factors whichever is larger. For small field applications (i.e. eye treatments), 10 cm $\times$ 10 cm, or the largest field clinically available</td>
</tr>
</tbody>
</table>

† The reference depth can be chosen in the ‘plateau region’, at a depth of 3 g cm$^{-2}$, for clinical applications of a monoenergetic proton beam (e.g. for plateau irradiations).
2.3 A little touch of Monte Carlo simulation

This section presents briefly and qualitatively the basic concepts of Monte Carlo simulation methods applied to radiation transport. It is mainly adapted from Salvat (2014). For a more comprehensive introduction to Monte Carlo simulation applied to the transport of radiation, the reader is referred to Bielajew (2001) or Salvat (2014).

Monte Carlo methods are a class of numerical methods that rely on the repeated sampling of random numbers to obtain a numerical result. In Monte Carlo simulation of radiation transport, the track of a particle is viewed as a random sequence of free flights that end with an interaction event where the particle loses energy, suffers an angular deflection and, occasionally, produces secondary particles. That is, each step of a particle track is characterised by the following variables: (i) step length (or free path) between successive interaction events, (ii) type of interaction taking place, and (iii) energy loss and angular deflection in that particular event (and initial state of the secondary particles, if any). Each of these variables (either discrete or continuous) are sampled from a probability distribution function. These probability density functions are determined by the differential cross sections for the relevant interaction mechanisms. Thus, the accuracy of a Monte Carlo calculation is limited by the accuracy of the interaction models it is based on. The precision of the calculation, however, can always be improved by simulating a larger number of histories.

The simulation scheme described above, in which the track of a particle is simulated interaction by interaction, is known as detailed simulation. Such a simulation scheme is feasible for particles such as photons, which undergo a reasonably low number of interactions per track, but not for high-energy charged particles, which may undergo millions of collisions before stopping. Fortunately in the case of charged particles most of these collisions involve small energy losses and small angular deflections, so that the effect (i.e. energy loss and angular deflection) of many interactions can be summed up and described approximately in a single simulation step. In this simulation strategy, the total energy loss and angular deflection at the end of each step is calculated from macroscopic stopping and multiple Coulomb scattering theories, respectively, and not from differential cross sections. This condensed simulation strategy is called, according to the terminology introduced by Berger (1963), complete grouping or class I simulation scheme.

There is a third approach to the simulation of charged particle transport called mixed or class II simulation scheme (Berger 1963). This approach distinguishes between soft collisions (i.e. interactions with small energy loss and angular deflection) and hard collisions (i.e. interactions with a large

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1 The term *history*, or *event*, refers typically to the tracks of a primary particle and all its descendants.
energy loss or large angular deflection). Mixed simulation combines the
detailed simulation of hard events with condensed simulation of soft events.
The boundary between soft and hard events is typically set by user-definable
threshold values.

The Monte Carlo method applied to radiation transport yields, except
for its inherent statistical uncertainty, the same information as the solution
of the Boltzmann transport equation, with the same interaction model. The
advantage of Monte Carlo methods is that they are easier to implement,
especially in complex geometries. The drawback is its random nature: all
the results are affected by statistical uncertainties, which can be reduced
at the expense of increasing the number of histories simulated and, hence,
the computation time. In this work, Monte Carlo methods are used to solve
macroscopic problems (e.g. the calculation of the absorbed dose) through the
simulation of microscopic events (the interaction of radiation with matter).
Chapter 3

Spencer–Attix
water/medium
stopping-power ratios for
proton pencil beams

This chapter is based on Gomà et al. (2013). It describes the Monte Carlo calculation of Spencer–Attix water/medium stopping-power ratios for proton pencil beams, which are important for both the reference and relative dosimetry of proton pencil beam. This work calculates water/medium stopping-power ratios, as a function of depth and radial distance, for proton energies ranging from 30 to 350 MeV and typical detection materials in proton therapy such as air, radiochromic film, gadolinium oxysulfide, silicon and lithium fluoride. Furthermore, it investigates the effect on the water/air stopping-power ratios of track-ends, particles heavier than protons, the mean excitation energy of water and the initial energy spread of the beam.

3.1 Introduction

The commissioning of scanned proton pencil beams requires: (i) reference dose measurements to calibrate the beam monitor chambers, (ii) relative dose measurements, i.e. depth-dose curves and lateral dose profiles, to feed the treatment planning system, and (iii) field-specific dose distributions measurements to validate the dose distribution predicted by the treatment planning system.

According to IAEA TRS-398 (see section 2.2.4), the absorbed dose to water under reference conditions should be measured in water with a cylindrical or plane-parallel ionization chamber. Depth-dose curves should also be measured in water (Andreo et al. 2000), with a large-diameter plane-parallel
ionization chamber (Jones et al. 2007). Lateral dose profiles are typically measured with high spatial resolution detectors, such as radiochromic films (Gillin et al. 2010) or scintillating screens coupled to a CCD camera (Pedroni et al. 2005). In what follows, and for the sake of simplicity, we will refer to these latter detectors as scintillating screens. Alternatively, lateral dose profiles may also be measured with a small volume ionization chamber (Gillin et al. 2010, Schwaab et al. 2011). Finally, field-specific dose distributions are typically measured with two-dimensional detectors such as ionization chamber matrices (Karger et al. 2010), radiochromic films (Albertini et al. 2011) or scintillating screens (Boon et al. 2000).

All these measurements, performed with different detectors and detection materials, will most likely be converted to absorbed dose to water. To correctly perform this step, it is essential to know the water/medium stopping-power ratio of the detection material and the perturbation correction factor of the detector. This chapter addresses the calculation of the water/medium stopping-power ratios ($s_{w,med}$) for proton pencil beams, which are a property of the detection material and the radiation field. The calculation of perturbation correction factors, which are a property of the detector and the radiation field, will be addressed in chapter 6 for ionization chambers.

In the field of proton therapy, the largest contributions to the calculation of stopping-power ratios have historically focused on the water/air stopping-power ratio ($s_{w,air}$), because of its importance for reference dosimetry. Medin & Andreo (1997) calculated $s_{w,air}$ values for monoenergetic proton beams from 50 to 250 MeV with their self-developed Monte Carlo code PETRA—where nuclear inelastic processes were taken into account but only protons (both primary and secondary) and delta-ray electrons were tracked. They found delta-ray electrons should be included in the calculation of $s_{w,air}$ whereas alpha particles could be omitted. Later, Laitano & Rosetti (2000) calculated $s_{w,air}$ values for proton beams with a realistic energy spectra—with the FLUKA Monte Carlo code—and they found no significant differences with $s_{w,air}$ values obtained for monoenergetic beams. Finally, IAEA TRS-398 derived the $s_{w,air}$ values for passively-scattered proton beams.

Based on these past results, the aim of this chapter is to use Monte Carlo simulations:

1. To calculate $s_{w,med}$ values for the detection materials most commonly used in the dosimetry of proton pencil beams. These detection materials are: air (ionization chambers), radiochromic film (Gafchromic EBT2/EBT3 active layer\(^1\)) and gadolinium oxysulfide ($\text{Gd}_2\text{O}_2\text{S}:\text{Tb}$, a scintillating material). Silicon (Si) and lithium fluoride ($\text{LiF}$) were also

\(^1\)According to the manufacturer, the active layers of EBT2 and EBT3 films are identical. In what follows, and for the sake of simplicity, we will refer to the EBT2/EBT3 active layer by simply EBT2.
3.2 Materials and methods

This chapter calculates water/medium stopping power ratios by means of the Spencer–Attix cavity theory, i.e. using equation (2.34). An upper limit for $E_{\text{cut}}$ is typically defined as the mean energy of the $i$-th particle with a sufficient residual range to cross the cavity. In this work, we set the size of the cavity equal to the typical mass-thickness of a plane-parallel ionization chamber cavity, i.e. $2.5 \cdot 10^{-4} \text{ g cm}^{-2}$. This setting leads to an upper limit for $E_{\text{cut}}$ of 10 keV for electrons, 175 keV for protons, 250 keV for alphas, etc. For simplicity, we set $\Delta = 10 \text{ keV}$ for electrons and $E_{\text{cut}} = 100 \text{ keV}$ for protons and heavier particles.

The calculation of the $s_{\text{w,med}}$ values was performed ‘off-line’. That is, we first calculated the distribution of the fluence with respect to the energy with Monte Carlo simulations and, afterwards, we calculated the $s_{\text{w,med}}$ values using equation (2.34). To overcome the potential deficiencies of an ‘off-line’ calculation, we used a dense ($\sim 10^3$) logarithmic energy binning. For the Monte Carlo simulations, we used GAMOS (Arce et al. 2014)—a Monte Carlo simulation software framework based on the GeANT4 toolkit. As a reference beam, we simulated a zero-emittance beam (zero initial lateral spread and zero initial angular spread) with a zero initial energy spread impinging on a sufficiently large (15 cm-radius) cylindrical water phantom. We used the $QGSP\_BIC\_EMY$ physics list (Cirrone et al. 2009), which combines the electromagnetic standard model for the electromagnetic processes, the binary cascade model for the hadronic inelastic processes, and an accurate tracking of electrons, hadrons and ions for dosimetry purposes. These physics settings have been proved to be suitable for the simulation of proton therapy beams (Zacharatou-Jarlskog & Paganetti 2008). We set the

included for completeness. Special attention was paid to $s_{\text{w,air}}$ because of its importance in reference dosimetry.

2. To extend the energy range from 30 to 350 MeV, to take into account the upcoming generation of proton therapy beam delivery systems.

3. To investigate the influence of particles heavier than protons and track-ends on the calculation of the stopping-power ratios.

4. To investigate the effect of the initial energy spread of the beam on the stopping-power ratios.

5. To investigate the dependence of $s_{\text{w,med}}$ on the radial distance (perpendicular to the beam direction). This last point was inspired by the results of Grassberger & Paganetti (2011) showing an increased LET in the penumbra region of clinical proton beams.
production cuts for photons, electrons and positrons to 2.5\,\mu m—to be consistent with our setting for the size of the cavity. We scored the (averaged) fluence of charged particles in a disc of water of 0.1\,mm of thickness and 10\,cm of radius, perpendicular to the beam axis. We chose a sufficiently large radius to capture all the secondary charged particles scattered at large angles due to inelastic nuclear interactions. As mentioned before, the fluence was scored in a dense ($\sim 10^3$) set of logarithmic energy bins, from $E_{\text{cut}}$ to $E_{\text{max}}$. We run as many particles as needed to achieve a standard statistical uncertainty in the final $s_{w,\text{med}}$ values lower than 0.1\%. The total uncertainty, however, is much larger and it is mainly due to the uncertainty in the mean excitation energy values ($I$-values) of the different media. This point will be discussed later.

For the calculation of $s_{w,\text{med}}$ using equation (2.34), we first considered only the fluence of protons and electrons (Medin & Andreo 1997)—the influence of heavier particles is investigated later. For all materials except for water, we took the mass electronic stopping powers ($S_{el}/\rho$) for protons and electrons directly from ICRU Report No. 49 (Berger et al. 1993) and ICRU Report No. 37 (Berger et al. 1984), respectively. When not tabulated, we calculated them with the Bragg additivity rule as suggested in ICRU 37, i.e. taking the $I$-values for the condensed phase of the elements in the compound. For water, however, we took the $I_w$-value suggested by Andreo et al. (2013) ($I_w = 78$\,eV), instead of the current ICRU 37 and ICRU 49 recommendation ($I_w = 75$\,eV). Finally, the restricted linear electronic stopping powers ($L_\Delta$) were calculated from $S_{el}$ as suggested in ICRU 49.

We studied the effect of particles heavier than protons and track-ends on the calculation of the water/air stopping-power ratio. In this case, all the charged particles that crossed the cavity were scored. The calculation of the water/air stopping-power ratio included alpha particles and all the ions with tabulated ($S_{el}/\rho$) values in ICRU Report No. 73 (Bimbot et al. 2005, Sigmund et al. 2009). These were the isotopes of lithium ($^6\text{Li}$, $^7\text{Li}$, $^8\text{Li}$), beryllium ($^6\text{Be}$, $^7\text{Be}$, $^9\text{Be}$, $^{10}\text{Be}$), boron ($^8\text{B}$, $^{10}\text{B}$, $^{11}\text{B}$, $^{12}\text{B}$, $^{13}\text{B}$), carbon ($^{10}\text{C}$, $^{11}\text{C}$, $^{12}\text{C}$, $^{13}\text{C}$, $^{14}\text{C}$, $^{15}\text{C}$), nitrogen ($^{12}\text{N}$, $^{13}\text{N}$, $^{14}\text{N}$, $^{15}\text{N}$, $^{16}\text{N}$, $^{17}\text{N}$), oxygen ($^{13}\text{O}$, $^{14}\text{O}$, $^{15}\text{O}$, $^{16}\text{O}$, $^{17}\text{O}$, $^{18}\text{O}$, $^{19}\text{O}$), fluorine ($^{17}\text{F}$, $^{18}\text{F}$, $^{19}\text{F}$) and neon ($^{20}\text{Ne}$). We included them in equation (2.34) as follows: for alpha particles we calculated $L_\Delta$; for heavier ions we assumed $L_\Delta \approx S_{el}$. This assumption is based on the fact that, for a given energy, the heavier the projectile, the lower the energy lost in a single collision with an electron in the medium (see equation (2.21)), so the smallest the difference between $L_\Delta$ and $S_{el}$. In case this approximation was not sufficiently accurate, this would result in an overestimation of the contribution of these heavier ions to $s_{w,\text{air}}$.

The effect of the track-ends was simply assessed by calculating $s_{w,\text{air}}$
3.3 Results and discussion

3.3.1 Without the track-end term, i.e.

\[ s_{w,\text{air}} = \sum_i \int_{E_{\text{cut}}^i}^{E_{\text{max}}^i} \Phi_w^i(E) \frac{(L_{\Delta}(E)/\rho)_w^i}{(L_{\Delta}(E)/\rho)_{\text{air}}^i} dE \]  

(3.1)

and comparing with the full equation (2.34). In this case, only the fluence of protons and electrons was taken into account.

We also investigated the effect of the initial energy spread of the beam on the \( s_{w,\text{air}} \) values in depth. We investigated a Gaussian initial (relative) energy spread, \( \sigma_E/E \), of 1%, which is representative of the values that can nowadays be achieved in modern proton therapy facilities (Clasie et al. 2012).

Finally we studied \( s_{w,\text{med}} \) as a function of the radial distance (perpendicular to the beam direction) at the depth of \( R_{80}/2 \), which is a depth with a broad halo of secondary protons for all energies (Pedroni et al. 2005). In this case, the scoring volume was divided in concentric rings of width equal to 0.5 \( \sigma_{\text{MCS}} \), where \( \sigma_{\text{MCS}} \) is the standard deviation of the lateral spread of the beam in depth due to multiple Coulomb scattering (MCS). \( \sigma_{\text{MCS}} \) was calculated at the depth of \( R_{80}/2 \) using the generalized Fermi-Eyges multiple scattering theory (Safai et al. 2008).

3.3 Results and discussion

Figure 3.1(a) shows the Spencer–Attix \( s_{w,\text{air}} \) values as a function of depth in water for different proton energies (30, 70, 150, 230 and 350 MeV). The depth in water is normalized to the range \( (R_{80}) \) of the proton beam. The numerical values are shown in table 3.1. As in Medin & Andreo (1997), it was found that the peak-to-plateau ratio decreases with increasing energy—from 2.5% for 30 MeV beams to 1% for 350 MeV beams. This is due to the range straggling in water, which makes the proton energy spectrum at the Bragg peak region much broader for high energies than for low energies.

Figure 3.1(b) shows a comparison of the Spencer–Attix \( s_{w,\text{air}} \) values, for a 150 MeV beam, obtained in this work with GEANT4 and the values published by Medin & Andreo (1997) using PETRA. When using the same input data \( (I_w = 75 \text{ eV}) \), an excellent agreement (within 0.1%) was found between the two Monte Carlo codes. When using \( I_w = 78 \text{ eV} \), we found differences from 0.6% in the plateau region and up to 1% in the Bragg peak region. As already pointed out by other authors (Andreo 2009, Henkner et al. 2009, Vatnitsky et al. 2011), the uncertainty in the \( I \)-values is currently the largest source of uncertainty in the \( s_{w,\text{air}} \) values. For relative dosimetry purposes however, the absolute \( s_{w,\text{air}} \) values are not so critical: the only relevant quantities are the relative \( s_{w,\text{air}} \) values along the beam range or, in other words, the peak-to-plateau ratio. Still, it was found that \( I_w \) has a noticeable effect on
Figure 3.1: (a) Spencer–Attix $s_{w,\text{air}}$ values as a function of depth for proton beams of initial energy 30, 70, 150, 230 and 350 MeV. The values correspond to $I_w = 78\,\text{eV}$. (b) Comparison of the $s_{w,\text{air}}$ values obtained in this work with the values published by Medin & Andreo (1997) for a 150 MeV proton beam.
3.3. Results and discussion

Table 3.1: Spencer–Attix $s_{w,\text{air}}$ values as a function of depth for proton beams of initial energy 30, 70, 150, 230 and 350 MeV. The values correspond to $I_w = 78$ eV.

<table>
<thead>
<tr>
<th>Depth/R$_{80}$ (cm)</th>
<th>Energy (MeV)</th>
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The peak-to-plateau ratio. For instance, for the 30 MeV beam, the peak-to-plateau ratio ranged from 2.8% (for $I_w = 75$ eV) to 2.0% (for $I_w = 78$ eV); for the 350 MeV beam, it ranged from 0.9% to 0.7%. The effect of the $I$-values on $s_{w,\text{air}}$ decreases with increasing energy. This is due to the fact that, the higher the energy of the projectile, the less relevant the $I$-value in the mass electronic stopping power of the projectile.

Figure 3.2 shows the distribution of the fluence of charged particles in water with respect to the energy generated by a proton beam of initial energy 150 MeV at the depth of $R_{80}/10 = 1.6$ cm. It was found that the main con-

Table 3.2: Relative per cent contribution of the different charged particles to the absorbed dose to water and, within parenthesis, relative per cent contribution of the track-ends to the dose deposited by that particle. The plateau region is represented by the depth of 0.1 $R_{80}$; the peak region, by 0.984 $R_{80}$, which corresponds roughly to the depth of the maximum.

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Protons 85.9 (0.0) 100 (0.2) 79.6 (0.0) 91.2 (0.0) 77.3 (0.0) 87.0 (0.0)
Electrons 13.6 (39) 0.0 (78) 19.2 (26) 8.6 (54) 20.7 (23) 12.5 (40)
Others 0.5 (0.1) 0.0 (3.0) 1.2 (0.5) 0.2 (0.3) 2.0 (0.4) 0.5 (0.4)
Figure 3.2: Distribution of the fluence of charged particles in water with respect to the energy per incident proton of initial energy 150 MeV at the depth of $R_{80}/10 = 1.6$ cm.

Distribution to the fluence comes from both protons and electrons; whereas the fluence of heavier particles is several orders of magnitude lower. Figure 3.2 also shows that the fluence of protons is clearly dominated by the primary protons and the fluence of electrons is clearly dominated by the proton-generated secondary electrons. The latter is shown by the drastic reduction of the electron fluence for $E > W_{max}$, where $W_{max}$ is the largest possible energy loss of a proton in single collision with a free electron (2.21); in this case, $W_{max} \sim 300$ keV. The major contribution of protons and electrons to the fluence does translate into a major contribution to the absorbed dose to water, as shown in table 3.2—where the relative contribution to $D_w$ from the different charged particle species is shown. The significant contribution of the electrons to both the fluence and the absorbed dose to water, however, does not translate into a significant contribution to the $s_{w,air}$ values.

Figure 3.3 shows the effect of including different charged particles (protons; both protons and electrons; and all charged particles) in the calculation of $s_{w,air}$ for different proton energies (30, 150 and 350 MeV). Systematic differences of the order of 0.1% were found when including electrons into equation (2.34), but no further significant differences were found when including the rest of particles heavier than protons. A similar behaviour was found for the track-ends. Table 3.2 also shows the relative contribution of the track-
3.3. Results and discussion

Figure 3.3: Spencer–Attix $s_{w,\text{air}}$ values as a function of depth for proton beams of initial energy 30, 150 and 350 MeV. The solid lines include only protons, the dashed lines include protons and electrons, and the chain lines include all charged particles.

ends to the dose deposited by each type of particle, within parenthesis. It was found that, although electron track-ends can deposit up to 80% of the total dose deposited by the electrons, the minor role of the electrons in the $s_{w,\text{air}}$ values makes the contribution of these track-ends negligible. For protons and heavier particles, the contribution of the track-ends to $D_w$ (and therefore to $s_{w,\text{air}}$) was found to be negligible—at least for the cut-off energy of $E_{\text{cut}} = 100 \text{ keV}$. Here, it is worth commenting on the need of including electrons in the calculation of the $s_{w,\text{air}}$ values. Medin & Andreo (1997) compared the Bragg-Gray $s_{w,\text{air}}$ values for protons with the Spencer–Attix $s_{w,\text{air}}$ values including both protons and electrons and they found differences of about 0.5%. This work compares the Spencer–Attix $s_{w,\text{air}}$ values including protons and both protons and electrons and it found differences of only 0.1%. This leads to the conclusion that, when using $L_\Delta$ in the cavity integral, as in equation (2.34), the inclusion of electrons in the calculation of $s_{w,\text{air}}$ is, to a very good approximation, not necessary.

Figure 3.4 shows the effect of the initial energy spread of the beam on the $s_{w,\text{air}}$ values as a function of depth in water for different proton energies (30, 150 and 350 MeV). A relative initial energy spread of 1% is compared
to a zero initial energy spread. We found differences up to 0.5\% in the Bragg peak region and no significant differences in the plateau. We also found the effect of the initial energy spread decreases with increasing energy. This is due to the fact that, at low energies, the total energy spread at the Bragg peak region is dominated by the initial energy spread of the beam whereas, at high energies, it is dominated by the range straggling in water. Furthermore, for the highest energy beams—meant for proton radiography (Depauw & Seco 2011)—one could argue that the initial energy spread of the beam has no effect on their relative dosimetry, since only the plateau region is used clinically. However, attention should be paid to low energy beams, where a narrow initial energy spread is technically more challenging—at least for cyclotron-based facilities—and its effect on the relative dosimetry should not be overlooked.

Figure 3.5 shows the $s_{w,\text{med}}$ values as a function of depth in water for different detection materials (air, EBT2, Gd$_2$O$_2$S:Tb, Si, LiF) and different proton energies (30, 150 and 350 MeV). The $s_{w,\text{med}}$ values are normalized to the entrance ($R_{80}/10$) value. Table 3.3 shows the absolute numerical values—for EBT2, gadolinium oxysulfide, Si and LiF—for proton beams of initial energy 30, 70, 150, 230 and 350 MeV. The numerical values for
Figure 3.5: Spencer–Attix $s_{w,med}$ values as a function of depth for different detection materials (air, EBT2, Gd$_2$O$_2$S:Tb, Si and LiF) and different proton energies: (a) 30 MeV, (b) 150 MeV and (c) 350 MeV. The $s_{w,med}$ values are normalized to the entrance value.
Table 3.3: Spencer–Attix $s_{w,\text{med}}$ values as a function of depth for different detection materials (EBT2, Gd$_2$O$_2$S:Tb, Si and LiF) and different proton energies (30, 70, 150, 230 and 350 MeV).

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$R_{80}$ (cm) 0.90  4.11  15.87  31.92  66.62

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$R_{80}$ (cm) 0.90  4.11  15.87  31.92  66.62
### Silicon

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$R_{80}$ (cm) | 0.90 | 4.11 | 15.87 | 31.92 | 66.62 |

### Lithium fluoride

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$R_{80}$ (cm) | 0.90 | 4.11 | 15.87 | 31.92 | 66.62 |
air are given in table 3.1. It was found that the $s_{w,\text{med}}$ values for air and EBT2 were quite constant (within 2.5%) along all depths. For lithium fluoride, the peak-to-plateau ratio went up to 5% (for 30 MeV). For silicon, we found peak-to-plateau ratios from 17% (for 30 MeV) down to 6% (for 350 MeV). Finally, for gadolinium oxysulfide, we found peak-to-plateau ratios from almost 60% (for 30 MeV) down to almost 20% (for 350 MeV). From these results, one could conclude that both air and EBT2 active layer seem to be appropriate detection materials for depth-dose measurements in water; LiF seems also to be acceptable given the typical uncertainties associated with thermoluminescent dosimetry; while the use of silicon diodes should be discouraged—gadolinium oxysulfide is never used for this kind of measurements. Nevertheless, it is worth pointing out that: (i) the $s_{w,\text{med}}$ values assume that the detection material does not perturb the fluence in the medium, so a constant $s_{w,\text{med}}$ along all depths does not imply that the perturbation factor of the detector will also be constant at all depths—see, for instance, the measurement of depth-dose curves with a Farmer-type ionization chamber or with radiochromic films (Angellier et al. 2011); and (ii) a constant $s_{w,\text{med}}$ and a constant detector perturbation factor at all depths means that the relationship between the absorbed dose to water and the absorbed dose to medium ($D_{\text{med}}$) is constant at all depths, but this does not imply that the relationship between $D_{\text{med}}$ and the detector reading/signal is also constant—see, for instance, the quenching effect in radiochromic films (Kirby et al. 2010).

Figure 3.6 shows the $s_{w,\text{med}}$ values as a function of the radial distance (perpendicular to the beam axis) for different detection materials (air, EBT2, Gd$_2$O$_2$S:Tb, Si, LiF) and different proton energies (30, 150 and 350 MeV) at the depth of $R_{80}/2$. The $s_{w,\text{med}}$ values are normalized to the central axis value. The radial distance is normalized to the lateral spread of the beam due to multiple Coulomb scattering ($\sigma_{\text{MCS}}$) at that depth of $R_{80}/2$. It was found that relative $s_{w,\text{med}}$ values start to differ from unity with increasing radial distance. This is due to the fact that, the larger the radial distance, the larger the relative contribution of secondary protons (with a much lower energy) to the total proton fluence, so the lower the mean energy of the spectrum. Similar results were reported by Andreo & Brahme (1981) for clinical electron beams. The region of clinical interest is the one where the absorbed dose to water has a non-negligible value—this is shown by the relative dose histogram plotted against the right axis in figure 3.6. Within this region, it was found that the $s_{w,\text{med}}$ values for air, EBT2 and LiF were constant along the radial distance (within 0.5% in the worst case scenario), and also for silicon (within 1%). For gadolinium oxysulfide, the tail-to-center ratio went from 1% (for 30 MeV) up to 3% (for 150 and 350 MeV). From these results, one could argue that scintillating screens might not be the most suitable detectors for lateral dose profiles measurements in depth. However, this kind of detectors are typically used to measure the lateral dose profiles
Figure 3.6: Spencer–Attix $s_{w,med}$ values (plotted against the left axis) and histogram of the absorbed dose to water (plotted against the right axis) as a function of radial distance for different detection materials (air, EBT2, Gd$_2$O$_2$S:Tb, Si and LiF) and different proton energies: (a) 30 MeV, (b) 150 MeV and (c) 350 MeV. Both $s_{w,med}$ values and dose values are normalized to the central axis value.
in air. In this case, the number of secondary protons scattered at large radial distances is much smaller and, hence, the relative stopping-power ratios along the radial distance are likely to remain constant.

3.4 Conclusions

This chapter calculated the Spencer–Attix water/medium stopping-power ratios for the dosimetry of clinical proton pencil beams. From the results obtained for \( s_{w, air} \), it was found that protons are, to a very good approximation, the only particles that need to be included in the calculation of the stopping-power ratios. The inclusion of electrons systematically increases the \( s_{w, air} \) values by 0.1%, whereas the inclusion of track-ends and particles heavier than protons does not have any effect on the \( s_{w, air} \) values.

In contradistinction, the choice of the \( I \)-values has a large effect on the \( s_{w, air} \) values—not only on the absolute values necessary for reference dosimetry, but also on the relative values (peak-to-plateau ratio) necessary for relative dosimetry. A difference of 3 eV in \( I_w \) results in a difference in the \( s_{w, air} \) values of approximately 0.6% in the plateau region and in an additional difference from 0.2% (350 MeV) to 0.7% (30 MeV) in the Bragg peak region. Clearly, the uncertainty in the \( I \)-values is nowadays the largest source of uncertainty in the stopping-power ratios.

Despite this uncertainty, a correction is still needed for depth-dose measurements to compensate for the different \( s_{w, med} \) values between the plateau and the Bragg peak region. The most suitable detection materials for depth-dose measurements in water were found to be air and EBT2 active layer. Based on the calculations made with \( I_w = 78 \) eV, a correction from roughly 1% (350 MeV) to 2.5% (30 MeV) should be used in the Bragg peak region for these two detection materials. The corrections needed for LiF—from roughly 2% (350 MeV) to 5% (30 MeV)—are also acceptable given the typical uncertainties associated with thermoluminiscent dosimetry. The use of silicon and gadolinium oxysulfide for depth-dose measurements in water should be discouraged.

In addition, the initial energy spread of the beam has little effect (<0.5%) on the \( s_{w, air} \) values in depth. It is therefore believed that, given the overall uncertainties, a single (already energy-dependent and depth-dependent) correction could be used, irrespective of the initial energy spread of the beam.

As for in-depth lateral dose profiles and field-specific dose distributions, all the studied detection materials—except for gadolinium oxysulfide—would be appropriate for these kinds of measurements. In the case of gadolinium oxysulfide, it is believed it could still be used for lateral dose profiles and field-specific dose distribution measurements in air.

Overall, it was found that proton radiography beams are more forgiving
to relative dosimetry subtleties whereas very low energy beams—such as
30 MeV beams—are more demanding, so special attention should be paid
to their relative dosimetry.
Chapter 4

Reference dosimetry vs Faraday cup dosimetry of proton pencil beams

Before addressing the Monte Carlo calculation of beam quality correction factors (chapter 6), chapters 4 and 5 describe the acquisition of some of the experimental data that will be used later to validate these Monte Carlo calculations.

This chapter is based on Gomà et al. (2014). It presents a comparison between ionization chamber dosimetry based on IAEA TRS-398 and Faraday cup dosimetry of proton pencil beams. Whereas ionization chamber dosimetry determines the absorbed dose to water at a point, Faraday cup dosimetry determines the number of protons impinging in a surface (i.e. the integrated fluence). To compare these two independent dosimetry techniques, Monte Carlo simulations were performed to convert absorbed dose to water to proton fluence. The comparison between the two techniques was made in the frame of the beam monitor chamber calibration of a proton pencil beam scanning delivery system. That is, the results are presented in terms of monitor units (MU) per proton—the relevant quantity for beam monitor chamber calibration—which is inversely proportional to the absorbed dose to water per MU.

4.1 Introduction

As already mentioned in section 2.2.4, the IAEA TRS-398 Code of Practice for proton beams recommends the determination of the absorbed dose to water in the middle of a spread-out Bragg peak (see table 2.2). This recommendation is appropriate for proton beam delivery systems in which the calibration of the beam monitor chamber (BMC) has no influence on the shape (i.e. the flatness) of the SOBP, but only on the absolute output.
factor. In what follows, we will refer to this kind of beam delivery systems as ‘type I’. This is for instance the case of double-scattering systems (Engelsman et al. 2009), where both the energy and the weight of the different Bragg peaks that form the SOBP are set by the range-modulation system, or the Gantry 1 spot-scanning system at the Paul Scherrer Institute (PSI) (Pedroni et al. 1995).

However, since the publication of IAEA TRS-398, many different particle beam delivery systems have been developed and, as first pointed out by Jäkel et al. (2004) for the GSI carbon-ion beam delivery system, the recommendation of using a SOBP as a reference field is no longer always appropriate. In particular, it is not appropriate for those particle beam delivery systems in which, during the delivery of a SOBP, the BMC has to monitor the different proton energies independently. In these systems, the BMC should be calibrated for each individual pseudo-monoenergetic particle beam (Jäkel et al. 2004). In what follows, we will refer to this kind of beam delivery systems as ‘type II’. This is for instance the case of uniform scanning systems (Farr et al. 2008, Zheng et al. 2011) and the vast majority of spot-scanning and raster-scanning particle beam delivery systems (Jäkel et al. 2004, Pedroni et al. 2004, Gillin et al. 2010, Kooy et al. 2010).

In this chapter we address the beam monitor chamber calibration of type II proton beam delivery systems. Different approaches could be used to calibrate the BMC in these systems (Jones et al. 2007): absolute determination of the number of protons exiting the nozzle with a Faraday cup (Coray et al. 2002, Grusell et al. 1995, Lorin et al. 2008, Lin et al. 2009), absolute dosimetry with a water calorimeter (Gagnebin et al. 2010, Medin 2010, Sarfehnia et al. 2010) or reference dosimetry with a commercially-available ionization chamber (Andreo et al. 2000, Jäkel et al. 2004, Clasie et al. 2012). The intercomparison of independent dosimetry techniques is extremely useful in order to (i) confirm the integrity of the different dosimetry techniques, (ii) detect and eliminate systematic errors in the dosimetry process and (iii) independently check the entire dosimetry chain (Jones et al. 2007). Amongst the above-mentioned dosimetry techniques, only two of them are suitable for a routine clinical use: absolute dosimetry with a Faraday cup (FC) and reference dosimetry with an ionization chamber (IC). A comparison between these two techniques has been performed by Coray et al. (2002) for type I beam delivery systems. In this chapter, we compared these two dosimetry techniques for type II beam delivery systems.

4.2 Materials and methods

4.2.1 Beam monitor chamber calibration

Beam monitor chambers in proton beam delivery systems are typically air-filled parallel-plate ionization chambers. Since the detection material is
4.2. Materials and methods

air and the electronic stopping-power of protons in air \((S_{el})_{\text{air}}\) is energy-dependent (2.18), the BMC output signal, i.e. the number of monitor units (MU), per incident proton is expected to be also energy-dependent and, on a first approximation, proportional to \((S_{el})_{\text{air}}\).

Gantry 2 at PSI is a type II beam delivery system (Pedroni et al. 2004, 2011). The primary beam monitor chamber is a 18 cm \(\times\) 26 cm parallel-plate ionization chamber based on the design of Gantry 1 monitor chamber (Lin et al. 2009). The applied voltage (2000 V) is sufficiently high to make recombination in the BMC negligible (Lin et al. 2009). At PSI, the BMC has historically been calibrated in terms of MU per proton (MU/p) (Pedroni et al. 2005). This is an alternative, but equivalent, approach to the \(D_{w}\)-based calibration—the relationship between the two will be discussed below. In this work, we calibrated the BMC for energies ranging from 70 to 230 MeV, in 10 MeV energy steps.

4.2.2 Absolute dosimetry with a Faraday cup

A Faraday cup is a dosimetry device which allows for an absolute determination of the number of protons exiting the nozzle. The design of the FC at PSI is described in detail by Lin et al. (2009). With a FC, the BMC calibration in terms of MU/p is straightforward. We positioned the FC right at the exit of the nozzle and we delivered a pseudo-monoenergetic pencil beam. The lateral size of the FC is sufficiently large (diameter of 12.7 cm) to capture the whole pencil beam (2 mm < \(\sigma\) < 6 mm) (Safai et al. 2012). The number of MU was given by the treatment control system. The FC gives an absolute measurement of the charge collected in the detector absorber. The number of protons was directly determined from the measured charge. In general, the main problem of FC dosimetry is the effect of secondary electrons—either forward-scattered from the entrance window or back-scattered from the absorber. This problem is solved by a guard ring potential that pulls the forward-scattered electrons back to the entrance window and a magnetic field that pulls the back-scattered electrons back to the absorber (Lin et al. 2009).

4.2.3 Reference dosimetry with an ionization chamber

An alternative approach to the BMC calibration is the reference dosimetry with a commercially-available ionization chamber. Note that, “for clinical applications with a monoenergetic proton beam”, IAEA TRS-398 also allows for the determination of \(D_{w}\) in the plateau region, at a reference measurement depth \((z_{\text{ref}})\) of 3 g cm\(^{-2}\) (see table 2.2). Whether type II beam delivery systems fall or not into this category is unclear and could be subject to different interpretations. We personally believe that, in a type II beam delivery system, each pseudo-monoenergetic proton beam could be considered as a
“clinical application with a monoenergetic proton beam’. Therefore, in what follows, we will refer to this recommendation of $z_{\text{ref}}$ as the ‘IAEA TRS-398 reference measurement depth for monoenergetic proton beams’.

Consequently, in this chapter, we determined $D_w$ according to the IAEA TRS-398 reference conditions for monoenergetic proton beams—except for the fact that we chose a $z_{\text{ref}}$ of 2 g cm$^{-2}$ (instead of 3 g cm$^{-2}$), as it will be discussed below. That is, we delivered a pseudo-monoenergetic $10 \times 10$ cm$^2$ field and we determined $D_w$ in the plateau region with an ionization chamber (Jäkel et al. 2004). This method is very sensitive to set up errors and $z_{\text{ref}}$ should be carefully chosen. On the one hand, $z_{\text{ref}}$ should be as shallow as possible so as to minimize the steep dose gradient in the plateau region of low-energy proton beams. On the other hand, $z_{\text{ref}}$ should be deep enough so as to avoid the nuclear build-up region of high-energy proton beams. Taking these two points into account, it seems to be that $z_{\text{ref}}$ should be energy dependent—as it is, for instance, in the case of high-energy electron beams (Andreo et al. 2000). Nevertheless, one should also keep in mind that clinical proton beam delivery systems may have a large number of beam energies—i.e. beam qualities—to be commissioned (for example, as of today, Gantry 2 at PSI has 114 energies commissioned), so an energy-independent $z_{\text{ref}}$ is also advisable from a practical point of view. Bearing all these points in mind, in this work we chose a trade-off reference measurement depth of $z_{\text{ref}} = 2$ g cm$^{-2}$. Note that, at this $z_{\text{ref}}$, a set up error of 0.5 mm would lead to an error of almost 1% in the determination of $D_w$ for a 70 MeV proton beam—due to the steep dose gradient at this depth. Once $D_w$ was determined, we took the number of MU given by the treatment control system and, knowing the distance between adjacent spots ($\delta x, \delta y$), we determined the number of MU per unit area at the point of measurement ($\text{MU}/\delta x \delta y$). With this approach, the BMC calibration is given in terms of monitor units per dose-area product ($\text{MU}/D_wA$)—see chapter 7 below.

We used three different types of ionization chambers: an IBA FC65-G (IBA Dosimetry GmbH, Schwarzenbruck, Germany) Farmer-type cylindrical chamber of 3.1 mm of radius, a PTW 31010 (PTW-Freiburg, Freiburg, Germany) Semiflex-type cylindrical chamber of 2.75 mm of radius and a PTW 34045 Advanced Markus plane-parallel chamber, with an electrode spacing of 1 mm (see table 6.2). The two cylindrical chambers were calibrated in terms of $D_w$ in a $^{60}$Co-beam at the Swiss Federal Institute of Metrology METAS (Bern-Wabern, Switzerland), a Primary Standard Dosimetry Laboratory. The plane-parallel chamber was cross-calibrated against the Farmer chamber in Gantry 1, i.e. in the middle of a SOBP. Note that, as pointed out in section 2.2.4, the $k_Q$ factors tabulated in IAEA TRS-398 are calculated from monoenergetic proton beam data. Their validity in a SOBP is based on the assumption that, for a given residual range, the different spectrum of charged-particles between a SOBP and a monoenergetic beam has a negligible influence on $s_{w,\text{air}}$. Thus, strictly speaking, the $k_Q$ factors
tabulated in IAEA TRS-398 are more suitable for monoenergetic beams than for SOBP fields.

Last but not least, it is worth commenting on the recombination effect in the ionization chambers. The proton beam at PSI is accelerated with a superconducting cyclotron. The cyclotron delivers a beam which is pulsed at a very high rate (pulse duration $\sim 1$ ns; time between pulses $\sim 10$ ns). The ion collection time in the ionization chamber is $\sim 100$ $\mu$s. When many pulses are delivered during the ion transit time (a factor $10^4$ in our case), the beam can be approximated as continuous (Attix 1986). In addition to that, the beam delivery in Gantry 2 is performed with the so-called spot-scanning technique (Pedroni et al. 2004), i.e. the proton beam is magnetically scanned across the plane perpendicular to the beam direction and it is delivered in “macro-pulses” called ‘spots’. The typical duration of a spot ranges from 1 to 10 ms and the “beam-off” time between spots is approximately 3 ms. When the pulse duration is long compared to the ion collection time (a factor 10 to 100 in our case), the beam can also be approximated as continuous (Lorin et al. 2008). Thus, both from the beam production and the beam delivery point of view, the proton beam in Gantry 2 can be approximated as a continuous beam—with regards to the ion recombination effect in the ionization chamber. In addition to that, from a delivery point of view, the beam is also scanned. Therefore, from the point of view of ion recombination in the ionization chamber, the proton beam in Gantry 2 can be considered a continuous–scanned beam. Lorin et al. (2008) proved that the ion recombination correction factor ($k_s$) for continuous beams can also be applied to continuous–scanned beams. Therefore, we calculated $k_s$—based on the IAEA TRS-398 formula for continuous beams—for an intermediate proton beam energy (150 MeV) and we assumed the $k_s$ factors to be constant within the energy range studied in this work.

4.2.4 Relationship between Faraday cup dosimetry and reference dosimetry

The two methods described above are reciprocal (Attix 1986). The FC-method consists of measuring a small field with a large detector; the IC-method consists of measuring a broad field with a small detector. The FC-method gives the BMC calibration in terms of MU/p; whereas the IC-method gives it initially in terms of $\mu$/D$_w$A. In order to compare these two methods, one needs a theoretical model that provides the integrated-dose per proton at $z_{ref}$—the integrated-dose is the integral of $D_w$ over the plane perpendicular to the beam direction (see chapter 7). This theoretical model will inevitably introduce an additional source of uncertainty in the comparison between the two methods. Since not only protons, but also electrons and other charged particles heavier than protons, contribute to $D_w$ in the plateau region of a monoenergetic proton beam (see table 3.2),
we used a theoretical model that takes all these particles into account. We performed Monte Carlo simulations with two different codes: Gamos v4.0.0, based on the Geant4 v4.9.5p02, and Fluka v2011.2b.6. For Geant4, we used the physics settings described in section 3.2. For Fluka, we used the default hadrontherapy physics settings. We calculated the integrated depth-dose curves, also called integral depth-dose curves by Pedroni et al. (2005), with Monte Carlo simulations. We adjusted the initial energy and the initial energy spread of the beam to match the experimental measurements. An accurate “fine-tuning” of the initial energy of the beam is especially important for low energy proton beams—where, for example, a difference of 1 MeV in a 70 MeV proton beam would lead to an error of up to 2% in the integrated-dose per proton at $z_{\text{ref}} = 2 \text{g cm}^{-2}$. An accurate “fine-tuning” of the initial energy spread of the beam is however not so critical, since the integrated-dose per proton in the plateau region is insensitive to the initial energy spread of the beam. In this work, we used the integrated-dose per proton calculated with Geant4 to convert the BMC calibration obtained with the IC-method (in terms of $\text{MU}/D_{w/A}$) to $\text{MU}/p$. The results obtained with Fluka were only used to estimate the uncertainty associated to the theoretical beam model.

4.3 Results and discussion

Figure 4.1 shows the beam monitor chamber calibration as a function of proton beam energy obtained with the Faraday cup and the three ionization chambers: Farmer, Semiflex and Advanced Markus. As expected, we found that the calibration curves follow, on a first approximation, the energy dependence of the mass electronic stopping-power of protons in air (Clasie et al. 2012).

Figure 4.2 shows the ratio between the BMC calibration obtained with the different ionization chambers and the BMC calibration obtained with the Faraday cup. For the plane-parallel ionization chamber, we found that the two methods differ by approximately 3% and that this difference is approximately constant along the entire energy range ($\pm 0.5\%$). For the cylindrical chambers, we found that the difference between the two methods is also constant ($\pm 0.5\%$) within the energy range from 100 to 230 MeV, but it reduces drastically in the energy interval from 100 to 70 MeV. In the view of these results, there are two points that need to be discussed separately: (i) the “absolute” discrepancy between the two methods, and (ii) the energy-dependence of such a discrepancy. We will begin with the latter.

Figure 4.2 shows that the BMC calibration obtained with the FC and the plane-parallel ionization chamber exhibit the same energy dependence. The fact that two totally independent methods give the same (relative) re-
4.3. Results and discussion

Figure 4.1: Plotted against the left axis, BMC calibration (in terms of MU/p) as a function of proton beam energy obtained with the Faraday cup, Farmer-type chamber, Semiflex chamber and Advanced Markus chamber. Plotted against the right axis, the mass electronic stopping-power of protons in air as a function of energy.

Results seems to indicate that a systematic measurement error is unlikely. In contradistinction, the BMC calibration curves obtained with the cylindrical chambers show a considerably different energy dependence at low energies (within the energy range of 70–100 MeV). This seems to indicate that, in this case, there is indeed a systematic error in the measurement. This error appears to be caused by the IAEA TRS-398 recommendation for the ‘position of the reference point of the chamber’. For proton beams, the recommendation is to position the reference point of the chamber at \( z_{\text{ref}} \) (see table 2.2) and to deal with the fluence perturbation factor of the chamber through the displacement correction factor \( \rho_{\text{dis}} \). This recommendation relies on the assumption that, in clinical proton beams, the dose gradients at \( z_{\text{ref}} \) are small. This assumption is valid in the middle of a SOBP (i.e. for type I beam delivery systems), but not in the plateau region of low-energy proton beams (i.e. for type II beam delivery systems). In this latter case, this wrong assumption results in a severe underestimation of the uncertainty of \( \rho_{\text{dis}} \) for cylindrical ionization chambers. IAEA TRS-398 takes \( \rho_{\text{dis}} = 1 \) and estimates an standard uncertainty of 0.2%, for both cylindrical and plane-parallel ionization chambers.
Figure 4.2: Ratio between the BMC calibration obtained with the different ionization chambers—Farmer, Semiflex and Advanced Markus—and the BMC calibration obtained with the Faraday cup.

However, when taking the effective point of measurement ($P_{\text{eff}}$) of our cylindrical ionization chambers into account, $P_{\text{eff}} \sim 2.2 \text{ mm}$ (Palmans 2006), the difference between $D_w(z_{\text{ref}})$ and $D_w(z_{\text{ref}} - P_{\text{eff}})$ is for a 70 MeV beam of the order of 4%. Hence, we repeated the Farmer chamber measurements but, this time, we positioned the effective point of measurement of the chamber at the reference measurement depth. We took $P_{\text{eff}} = 2.2 \text{ mm}$ (Palmans 2006). Figure 4.3 shows the ratio between the BMC calibration obtained with both Farmer and Advanced Markus ionization chambers and the BMC calibration obtained with the Faraday cup. For the Farmer chamber, two different scenarios are shown: (i) the reference point of the chamber ($P_{\text{ref}}$) positioned at $z_{\text{ref}}$, i.e. according to IAEA TRS-398 recommendations, and (ii) the effective point of measurement of the chamber positioned at $z_{\text{ref}}$. We found that, when positioning $P_{\text{eff}}$ at $z_{\text{ref}}$, the BMC calibration curve obtained with the Farmer chamber exhibits, to a good approximation, the same energy dependence than the BMC calibration curves obtained with the FC and the plane-parallel IC. Hence, these results seem to indicate that, for the particular case of pseudo-monoenergetic proton beams, the effective point of measurement of the ionization chamber should be positioned at the reference depth—as in the case of high-energy electron and carbon-ion beams (Andreo et al. 2000).
Figure 4.3: Ratio between the BMC calibration obtained with different ionization chambers—Farmer and Advanced Markus—and the BMC calibration obtained with the Faraday cup. For the Farmer chamber, the BMC calibration is performed with both the reference point of the chamber positioned at $z_{\text{ref}}$ (dashed line) and the effective point of measurement of the chamber positioned at $z_{\text{ref}}$ (solid line).

Figure 4.3 also shows that the “absolute” difference between the FC and IC techniques is of the order of 3% ($\pm 1\%$). In order to assess the agreement between these two techniques, we first have to discuss the uncertainties involved in the comparison. Based on Coray et al. (2002), we estimated an standard uncertainty of $u = 0.5\%$ to the FC-technique—this value is of the order of the one reported by Grusell et al. (1995) for their particular Faraday cup design. For the IC-technique we distinguish between plane-parallel and cylindrical ionization chambers.

For the plane-parallel ionization chamber different series of measurements, spread over a 6 month-period, showed that the statistical standard uncertainty in the experimental measurements (including setup errors) was $u = 0.4\%$. The standard uncertainty of the calibration factor, derived from a cross-calibration against the Farmer chamber, was estimated to be $u = 2.0\%$. Finally, we estimated the standard uncertainty of $k_{Q,Q_{\text{cross}}}$ to be $u = 0.1\%$, based on the typical variation of the $k_Q$ factors of plane-parallel ionization chambers with the residual range (Andreø et al. 2000). Note that here $k_{Q,Q_{\text{cross}}}$ has the explicit subscript $Q_{\text{cross}}$ to stress that the reference beam quality in the calibration factor is not $^{60}\text{Co}$ gamma radiation but a proton.
SOBP field of $R_{\text{res}} = 5 \text{ g cm}^{-2}$. All together, it led to a combined standard uncertainty in the determination of $D_w$ with the plane-parallel chamber of $u = 2.0\%$.

For the cylindrical ionization chambers different series of measurements, spread also over a 6 month-period, showed that the statistical standard uncertainty in the experimental measurements (including setup errors) was $u = 1.8\%$—this larger uncertainty is due to the fact that our positioning system for cylindrical ionization chambers is less accurate than the one for the plane-parallel IC. It is worth commenting that, when taking $P_{\text{eff}}$ into account, we estimated the standard uncertainty of $p_{\text{dis}}$ to be $u = 0.2\%$, as in used the IAEA TRS-398. The reason for that is the following. We estimated the uncertainty of $P_{\text{eff}}$ to be $\delta P_{\text{eff}} = 0.1 \text{ mm}$. For low-energy proton beams (worst case scenario) this $\delta P_{\text{eff}}$ results in $\delta D_w = 0.3\%$. Assuming a rectangular distribution of the uncertainty, the standard uncertainty of $p_{\text{dis}}$ is estimated to be $u = 0.2\%$. Hence, we estimated the combined standard uncertainty in the determination of $D_w$ with a cylindrical chamber to be $u = 2.7\%$.

Finally, there is an additional source of uncertainty in the theoretical beam model used to compare the two techniques. This uncertainty is, however, difficult to quantify. When comparing with other theoretical models used in the literature based exclusively on $(S_{\alpha})_w$ of the primary particles (Grusell et al. 1995, Jäkel et al. 2004, Pedroni et al. 2005), the differences in the integrated-dose per proton at $z_{\text{ref}} = 2 \text{ g cm}^{-2}$ are considerably large—up to 9% for the highest energies studied in this work. Nevertheless, when comparing with other Monte Carlo codes which also take electrons and particles heavier than protons into account, the differences seem to be much smaller. In this work, we found that the differences in the integrated-dose per proton (at $z_{\text{ref}} = 2 \text{ g cm}^{-2}$) between GEANT4 and FLUKA were smaller than 1%. The differences with MCNPX (Titt et al. 2012) seem also to be smaller than 1%. Hence, assuming a standard uncertainty in the integrated-dose per proton of $u = 1\%/\sqrt{3} = 0.6\%$, the combined standard uncertainty of the ratio between the BMC calibration curves obtained with FC and IC is: $u = 2.2\%$ for the plane-parallel ionization chamber and $u = 2.8\%$ for cylindrical ionization chambers.

Thus, based on this estimate, we could conclude that the FC and IC techniques agree with each other within two standard uncertainties. However, it is worth pointing out that the difference of approximately 3% between the calibration curves obtained with the two techniques is of systematic nature. The sources of this systematic difference are: (i) the collection efficiency of the Faraday cup, (ii) the accuracy of the theoretical beam model predicting the integrated-dose per proton at $z_{\text{ref}}$ and (iii) the $k_Q$ factors tabulated in IAEA TRS-398 for proton beams. Further research on these topics would definitely help to reduce the 3% gap between the two dosimetry techniques.

Finally it is worth discussing the results of other authors. Clasie et al.
4.4 Conclusions

In this chapter we compared two different techniques to calibrate the beam monitor chamber in type II beam delivery systems: absolute dosimetry with a Faraday cup and reference dosimetry with an ionization chamber. We found the calibration curves obtained with the two independent dosimetry techniques agree within two standard uncertainties. The difference of approximately 3% between the two curves was found to be constant along the entire energy range studied in this work (70–230 MeV). Further research needs to be done to reduce the uncertainties of both methods and to narrow down the gap between them.

For cylindrical ionization chambers, we found a systematic error in the determination of $D_w$, especially relevant for low-energy proton beams. This error arises from the IAEA TRS-398 recommendation of positioning the reference point of the chamber at the reference depth. The results obtained in this work seem to indicate that, for pseudo-monoenergetic proton beams, the effective point of measurement of cylindrical ionization chambers should be positioned at the reference depth—as in the case of high-energy elec-
tron and carbon-ion beams. It is beyond the scope of this work to propose new recommendations for the reference dosimetry of clinical proton beams. Nevertheless, given the results presented here, we believe that for the reference dosimetry of pseudo-monoenergetic proton beams the use of plane-parallel ionization chambers is preferable to the use of cylindrical ionization chambers—especially for low-energy proton beams.
Chapter 5

Experimental validation of beam quality correction factors for proton beams

This chapter is based on Gomà et al. (2015). It describes the experimental validation of the beam quality correction factors for proton beams tabulated in IAEA TRS-398 and the determination of beam quality correction factors of non-tabulated ionization chambers, based on the existing tabulated values. The experimental validation consists in comparing the reading of two ionization chambers under the same reference conditions in a proton beam quality $Q$ and a reference beam quality $^{60}$Co. This allows to experimentally determine the ratio between the beam quality correction factors of the two ionization chambers. These ratios are valuable experimental data to validate the beam quality correction factors calculated with Monte Carlo simulation in chapter 6.

5.1 Introduction

In this chapter we used a method based exclusively on ionometry to determine experimentally the ratio of $k_{Q,Q_0}$ factors of two ionization chambers (Palmans et al. 2001, 2002, González-Castaño et al. 2009). The method consists of comparing the reading of two ionization chambers under the same reference conditions in the beam qualities $Q$ and $Q_0$. Assuming a constant beam delivery, i.e. assuming $D_{w,Q}$ and $D_{w,Q_0}$ are constant, it follows from equation (2.45) that the ratio of $k_{Q,Q_0}$ factors of two ionization chambers is

$$\frac{k_{Q,Q_0}}{k_{Q_0,Q_0}} = \frac{M_{Q_0}/M_Q}{M_{Q_0}^{\text{ref}}/M_Q^{\text{ref}}}$$

(5.1)
That is, assuming a known reference $k_{Q,Q_0}^{ref}$, one could determine experimentally the $k_{Q,Q_0}$ of another ionization chamber. Note that from equation (2.46) it follows that the ratio of $k_{Q,Q_0}$ factors of two air-filled ionization chambers may also be expressed as the ratio of the perturbation correction factors in the beam qualities $Q$ and $Q_0$

$$\frac{k_{Q,Q_0}}{k_{Q_0}^{ref}} = \frac{p_Q/p_{Q_0}}{p_Q^{ref}/p_{Q_0}^{ref}}.$$  

(5.2)

This expression will be used later in the discussion of the results.

In this chapter we used this method to experimentally validate the $k_Q$ factors tabulated in IAEA TRS-398 for proton beams and to determine the $k_Q$ factors of non-tabulated ionization chambers (based on the already existing ones). We applied this method to both the reference conditions for modulated and monoenergetic proton beams (see table 2.2).

### 5.2 Materials and methods

The ratio between the $k_{Q,Q_0}$ factors of two ionization chambers is given by equation (5.1). Therein, the reading of the ionization chamber ($M$) is corrected for all the quantities of influence, except for the beam quality. The corrected reading is given by

$$M = M' k_T k_h k_{elec} k_{pol} k_s k_t$$  

(5.3)

where $M'$ is the uncorrected reading, $k_T$ is the correction factor for pressure and temperature, $k_h$ for humidity, $k_{elec}$ for electrometer, $k_{pol}$ for polarity and $k_s$ for ion recombination (Andreo et al. 2000). An additional correction factor $k_t$ was introduced to account for the decrease in the $^{60}$Co source activity with time. We calculated $k_T$ as described in IAEA TRS-398. No correction was applied for humidity ($k_h = 1$), as the measurements were performed in acclimatized rooms which ensured a humidity within 20–80%. The electrometer correction factor $k_{elec}$ was determined at the Swiss Federal Institute of Metrology METAS using a calibrated capacitance charged under an accurately measured voltage. Concerning $k_{pol}$, we used a fixed polarization for each ionization chamber so that $k_{pol}$ cancels out in equation (5.1). The recombination correction factor $k_s$ depends on the beam quality and it will be discussed below. Finally, for the $^{60}$Co beam $k_t = \exp (\lambda (t - t_0))$, where $t_0$ is an arbitrary reference time and $\lambda$ is the $^{60}$Co decay constant. For the proton beam $k_t = 1$.

In addition to $^{60}$Co and proton beam measurements, we also performed measurements in a $^{90}$Sr source (before and after each $^{60}$Co and proton beam measurement) to check the long-term stability of the ionization chambers.

Table 5.1 shows the list of ionization chambers used in this work, all of them being waterproof. We used two IBA FC65-G Farmer chambers, one
5.2. Materials and methods

Table 5.1: List of ionization chambers used in this work. The last column shows the number of chambers available for each model.

<table>
<thead>
<tr>
<th>Model</th>
<th>Geometry</th>
<th>Type</th>
<th>Active volume (cm³)</th>
<th>Voltage (V)</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBA FC65-G</td>
<td>cylindrical</td>
<td>Farmer</td>
<td>0.65</td>
<td>+500</td>
<td>2</td>
</tr>
<tr>
<td>IBA NACP</td>
<td>plane-parallel</td>
<td>NACP02</td>
<td>0.16</td>
<td>+200</td>
<td>1</td>
</tr>
<tr>
<td>PTW 23343</td>
<td>plane-parallel</td>
<td>Markus</td>
<td>0.055</td>
<td>+300</td>
<td>2</td>
</tr>
<tr>
<td>PTW 30013</td>
<td>cylindrical</td>
<td>Farmer</td>
<td>0.6</td>
<td>+400</td>
<td>1</td>
</tr>
<tr>
<td>PTW 31010</td>
<td>cylindrical</td>
<td>Semiflex</td>
<td>0.125</td>
<td>+400</td>
<td>1</td>
</tr>
<tr>
<td>PTW 34001</td>
<td>plane-parallel</td>
<td>Roos</td>
<td>0.35</td>
<td>+200</td>
<td>2</td>
</tr>
<tr>
<td>PTW 34045</td>
<td>plane-parallel</td>
<td>Advanced Markus</td>
<td>0.020</td>
<td>+300</td>
<td>2</td>
</tr>
</tbody>
</table>

IBA NACP02 chamber, two PTW 23343 Markus chambers, one PTW 30013 Farmer chamber, one PTW 31010 Semiflex chamber, two PTW 34001 Roos chambers and two PTW 34045 Advanced Markus chambers. All ionization chamber models, except for the PTW Advanced Markus, have tabulated $k_Q$ factors in IAEA TRS-398.

5.2.1 $^{60}$Co beam

The measurements in the $^{60}$Co beam were performed at METAS. The $^{60}$Co irradiation unit is a GE ALCYON II and has a dose rate at the reference point of measurement of about 1 Gy/min. We irradiated the ionization chambers according to the IAEA TRS-398 reference conditions for $^{60}$Co beams. That is, the measurement depth ($z_{ref}$) was 5 g cm$^{-2}$; the source-to-chamber distance 100 cm; and the field size at $z_{ref}$ $10 \times 10$ cm$^2$.

For each ionization chamber, we followed the exact same protocol: (i) we connected the IC to the electrometer and switched on the high voltage (HV) source at least 2 hours before the start of the measurements, (ii) we pre-irradiated the IC with 10 Gy, (iii) we performed $^{90}$Sr check-source measurements (sandwiched with leakage current measurements), and (iv) we performed 25 standard $^{60}$Co measurements (also sandwiched with leakage current measurements). For each single measurement we recorded the pressure and temperature in the vicinity of the ionization chamber. The humidity was recorded once during the measurement run.

Herein it is worth commenting on the ion recombination correction factor in the $^{60}$Co beam. For each chamber we performed standard $^{60}$Co measurements at different voltages, from the nominal voltage ($V_{max}$) down to 50 V and back again to $V_{max}$, in 50 V steps. After changing the HV, we waited at least 5 minutes before starting the next measurement. Based on Derkum (2003) and older ion recombination measurements in $^{60}$Co performed at METAS and analysed with the Boutillon method Boutillon (1998), we
determined $k_s$ by fitting the points of the linear part of the $1/M'$ vs $1/V$ curve and making $V \to \infty$.

### 5.2.2 Proton beam

The measurements in the proton beam were performed in Gantry 2 at PSI. As mentioned above, we studied both the reference conditions for modulated and monoenergetic proton beams. According to IAEA TRS-398, the reference field for modulated proton beams should be a spread-out Bragg peak (see table 2.2). We used a $10 \times 10 \times 10$ cm$^3$ SOBP with a distal range of $R_{80} = 20.40$ g cm$^{-2}$ and a practical range of $R_p = 20.96$ g cm$^{-2}$ (see figure 5.1). The ionization chambers were positioned at $z_{ref} = 15$ g cm$^{-2}$, which led to a residual range of $R_{res} = 5.96$ g cm$^{-2}$. The absorbed dose to water at $z_{ref}$ was 1 Gy and the field was delivered in approximately 60 s. In addition to that, we also irradiated the ionization chambers with a pseudo-monoenergetic $10 \times 10$ cm$^2$ field. We selected the energy of the pseudo-monoenergetic field ($E = 174$ MeV, according to ICRU 49) to match the energy of the most distal layer of the SOBP (see figure 5.1). The range of the pseudo-monoenergetic field was $R_{80} = 20.74$ g cm$^{-2}$ and the practical range $R_p = 20.93$ g cm$^{-2}$. Again, we positioned the ionization chambers at $z_{ref}$ of 15 g cm$^{-2}$, which led to a residual range of $R_{res} = 5.93$ g cm$^{-2}$. The absorbed dose to water at
5.3. Results and discussion

\( z_{\text{ref}} \) was approximately 0.35 Gy and the field was delivered in approximately 10 s. For \( R_{\text{res}} > 2 \text{ g cm}^{-2} \), small variations in \( R_{\text{res}} \) (of the order of 0.1 g cm\(^{-2}\)) have a negligible effect on \( k_Q \). Therefore, in what follows, we will refer to the \( Q \) studied in this work with the rounded up value of \( R_{\text{res}} = 6 \text{ g cm}^{-2} \). It should be mentioned that, according to IAEA TRS-398 recommendations, \( z_{\text{ref}} \) for a 174 MeV proton beam should be 3 g cm\(^{-2}\), instead of 15 g cm\(^{-2}\) (see table 2.2). Nevertheless, it should also be noted that the setup studied in this work is in good approximation equivalent to the IAEA TRS-398 reference conditions for a 109 MeV proton beam (where \( z_{\text{ref}} = 3 \text{ g cm}^{-2} \) leads to \( R_{\text{res}} = 6 \text{ g cm}^{-2} \)). In any case, the conclusions derived from this experiment do apply to pseudo-monoenergetic proton beams of \( R_{\text{res}} = 6 \text{ g cm}^{-2} \).

In the proton beam we followed the exact same protocol for each ionization chamber: (i) we connected the IC to the electrometer and switched on the HV-source at least 2 hours before the start of the measurements (during this time, the IC was continuously irradiated with the \(^{90}\text{Sr}\) source), (ii) we performed \(^{90}\text{Sr}\) check-source measurements (sandwiched with leakage current measurements), (iii) we pre-irradiated the IC with 10 Gy, (iv) we performed 20 SOBP measurements (sandwiched with leakage current measurements), and (v) we performed 20 pseudo-monoenergetic field measurements (sandwiched with leakage current measurements). For each single measurement we recorded the pressure and temperature in the vicinity of the ionization chamber. The humidity was monitored during the whole measurement run.

As above, it is worth discussing the ion recombination effect in the ionization chambers in the proton beam. The proton beam in Gantry 2 at PSI can be considered a continuous-scanned beam (see section 4.2). For every ionization chamber we performed pseudo-monoenergetic field measurements at different voltages, from \( V_{\text{max}} \) down to 50 V. We plotted \( 1/M' \) vs \( 1/V^2 \), we fitted a straight line and we determined \( k_s \) by making \( V \to \infty \). As a double-check, we also calculated \( k_s \) using the IAEA TRS-398 formula for continuous beams, which has been proven to be also valid for continuous-scanned beams (Lorin et al. 2008), and we obtained the same results. Indeed, the \( k_s \) factors obtained in our scanned proton beam were found to be comparable to those obtained in the \(^{60}\text{Co}\) beam, leading to corrections for ion recombination ranging from one to three per mille.

### 5.3 Results and discussion

Table 5.2 shows the experimental \( k_Q/k_Q^{\text{ref}} \) ratio for \( R_{\text{res}} = 6 \text{ g cm}^{-2} \) and for different ionization chambers. The average reading of the two Markus chambers is taken as reference. The first result that needs to be pointed out is that the differences between chambers of the same model are of the order of a few per mille; and they always agree within one standard uncertainty.
Table 5.2: Experimental $k_Q/k_Q^{ref}$ for different ionization chambers, with the average reading of the two PTW 23343 Markus chambers taken as reference. The proton beam quality is $R_{res} = 6 \text{ g cm}^{-2}$. The values within parenthesis correspond to one standard uncertainty in the last digit.

<table>
<thead>
<tr>
<th>Ionization chamber model</th>
<th>Serial number</th>
<th>$k_Q/k_Q^{ref}$ SOBP</th>
<th>$k_Q/k_Q^{ref}$ monoenergetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBA FC65-G #2640</td>
<td>1.032(2)</td>
<td>1.050(4)</td>
<td></td>
</tr>
<tr>
<td>IBA FC65-G #2641</td>
<td>1.032(2)</td>
<td>1.048(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 30013 #6557</td>
<td>1.030(2)</td>
<td>1.051(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 31010 #3153</td>
<td>1.030(2)</td>
<td>1.045(4)</td>
<td></td>
</tr>
<tr>
<td>IBA NACP02 #13501</td>
<td>0.985(2)</td>
<td>0.989(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 23343 #1876</td>
<td>1.000(2)</td>
<td>0.999(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 23343 #4335</td>
<td>1.000(2)</td>
<td>1.000(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 34001 #091</td>
<td>0.996(2)</td>
<td>1.006(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 34001 #1094</td>
<td>0.997(2)</td>
<td>1.007(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 34045 #515</td>
<td>0.996(2)</td>
<td>0.996(4)</td>
<td></td>
</tr>
<tr>
<td>PTW 34045 #516</td>
<td>0.994(2)</td>
<td>0.993(4)</td>
<td></td>
</tr>
</tbody>
</table>

Table 5.3: Theoretical and experimental $k_Q(R_{res} = 6 \text{ g cm}^{-2})$ for different ionization chambers. The $k_Q$ factor of the Markus chamber is taken as reference. The values within parenthesis correspond to one standard uncertainty in the last digit. The uncertainty estimate does not take into account the uncertainty of $k_Q^{ref}$.

<table>
<thead>
<tr>
<th>Ionization chamber model</th>
<th>Type</th>
<th>$k_Q$ IAEA TRS-398</th>
<th>Experimental $k_Q$ SOBP</th>
<th>Experimental $k_Q$ monoenergetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBA FC65-G</td>
<td>Farmer</td>
<td>1.040</td>
<td>1.034(2)</td>
<td>1.051(4)</td>
</tr>
<tr>
<td>PTW 30013</td>
<td>Farmer</td>
<td>1.030</td>
<td>1.032(2)</td>
<td>1.053(4)</td>
</tr>
<tr>
<td>PTW 31010</td>
<td>Semiflex</td>
<td>1.029</td>
<td>1.032(2)</td>
<td>1.047(4)</td>
</tr>
<tr>
<td>IBA NACP02</td>
<td>NACP</td>
<td>0.988</td>
<td>0.987(2)</td>
<td>0.991(4)</td>
</tr>
<tr>
<td>PTW 23343</td>
<td>Markus</td>
<td>1.002</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>PTW 34001</td>
<td>Roos</td>
<td>1.001</td>
<td>0.999(2)</td>
<td>1.009(4)</td>
</tr>
<tr>
<td>PTW 34045</td>
<td>Adv. Markus</td>
<td>–</td>
<td>0.997(2)</td>
<td>0.997(4)</td>
</tr>
</tbody>
</table>
Figure 5.2: Theoretical and experimental $k_Q(R_{res} = 6 \text{ g cm}^{-2})$ for different ionization chambers. The $k_Q$ factor of the Markus chamber is taken as reference. The error bars correspond to two standard uncertainties. The uncertainty estimate does not take into account the uncertainty of $k_{Q}^{ref}$.

Figure 5.2 shows a comparison between the $k_Q$ factors tabulated in IAEA TRS-398 and the $k_Q$ factors experimentally determined in this work, taking the $k_Q$ factor of the Markus chamber as reference. The numerical values are shown in table 5.3. For discussion purposes, the uncertainty values shown in figure 5.2 and table 5.3 do not take the uncertainty of $k_{Q}^{ref}$ into account, which is $u = 2.1\%$ (see table 2.1), but only the uncertainty associated to the experimental measurements.

Figure 5.2 shows that in the SOBP field there is a good agreement between the theoretical (i.e. tabulated in IAEA TRS-398) and experimental $k_Q$ factors for both cylindrical and plane-parallel ionization chambers—with the exception of the IBA FC65-G chamber, which will be discussed below. However, in the pseudo-monoenergetic field, the theoretical and experimental $k_Q$ factors do only agree (within two standard uncertainties) for plane-parallel chambers, but not for cylindrical chambers. For the IBA FC65-G chamber one could argue that the experimental $k_Q$ factor (determined in the pseudo-monoenergetic field) agrees with the theoretical value within three standard uncertainties ($k = 3$). However, for the PTW 30013 and the PTW 31010 chambers the discrepancy between the experimental and theoretical $k_Q$ fac-
tors cannot be explained by these means. Note from equation (5.1) that a higher $k_Q$ factor may be explained by a lower reading of the chamber in the user beam quality ($M_Q$). Therefore, the higher $k_Q$ factors obtained for cylindrical ionization chambers in pseudo-monoenergetic proton beam fields could be explained by the fact that, under these reference conditions, the reading of cylindrical ionization chambers is lower than it should. These results agree with the findings of chapter 4, where we pointed out that, for cylindrical ionization chambers in pseudo-monoenergetic fields, the IAEA TRS-398 recommendation of positioning the reference point of the chamber at the reference depth leads to a systematic underestimation of $D_w$, especially relevant for low $R_{res}$. Thus, the results of this chapter support the suggestion that, for pseudo-monoenergetic proton beams, the effective point of measurement ($P_{eff}$) of cylindrical ionization chambers should be positioned at the reference depth. Or, alternatively, dose gradient effects should be corrected when using cylindrical ionization chambers (Palmans et al. 2001). Note that, for plane-parallel ionization chambers, the reference point of the chamber is already defined to be at $P_{eff}$ (see table 2.2).

In SOBP fields, where dose gradients are small, the effect of $P_{eff}$ in cylindrical ionization chambers is minor. In this case figure 5.2 also shows that, when taking the $k_Q$ factor of the Markus chamber as reference, the experimental $k_Q$ factors of all the ionization chambers (except for the IBA FC65-G) agree with the theoretical values tabulated in IAEA TRS-398 within two standard uncertainties. In other words, we found that the tabulated values of all chambers, except for the IBA FC65-G, are consistent with each other. For the IBA FC65-G, we found that the experimental $k_Q$ factor is lower than the theoretical one by 0.6%. This result agrees with the results of Palmans et al. (2001) and chapter 4. Using equation (5.2), it can be shown that the ratio of $k_Q$ factors IBA FC65-G/PTW 30013 determined by Palmans et al. (2001) agrees with the result of this work within 0.1%. In chapter 4 we used an IBA FC65-G and a PTW 31010 chambers (i.e. the same ionization chamber models than in this chapter, but different serial numbers) simultaneously calibrated at the same PSDL (METAS) and we obtained $D_w$ values with the IBA FC65-G chamber that were approximately 1% lower than the ones obtained with the PTW 31010. Thus, the results of this chapter seem to indicate that (at least part of) the discrepancy between the IBA FC65-G and the PTW 31010 chambers observed in chapter 4 could be due to the fact that the tabulated $k_Q$ factor of the IBA FC65-G Farmer is not consistent with the tabulated $k_Q$ factor of the PTW 31010 Semiflex (and the rest of ionization chamber models studied here). Nonetheless, it should be mentioned that a discrepancy of 0.6% is well within the uncertainty of the $k_Q$ factors estimated in IAEA TRS-398 (see table 2.1).
5.4 Conclusions

In this chapter we presented a method to experimentally validate the $k_Q$ factors tabulated in IAEA TRS-398 for proton beams and to determine the $k_Q$ factors of non-tabulated ionization chambers, based on the already existing ones. We found that the tabulated $k_Q$ factors of all the ionization chambers studied (except for the IBA FC65-G) are consistent with each other; whereas the tabulated $k_Q$ factor of the IBA FC65-G is not consistent with the rest—the experimental value being 0.6% lower than the tabulated one. For the PTW 34045 Advanced Markus chamber, we found that $k_Q(R_{res} = 6 \text{ g cm}^{-2}) = 0.997(21)$ $(k = 1)$, based on the tabulated value of the PTW Markus chamber. Finally, concerning the reference dosimetry of pseudo-monoenergetic proton beams, this chapter provides arguments—in addition to the ones given by Palmans et al. (2001) and in chapter 4—in favour of positioning the effective point of measurement of cylindrical ionization chambers at the reference depth.
Chapter 6

Monte Carlo calculation of beam quality correction factors for proton beams

This chapter is based on Gomà et al. (2016). It describes the calculation of beam quality correction factors in monoenergetic proton beams, based on the Monte Carlo simulation of ionization chambers. It uses the Monte Carlo code \textsc{penh} and electronic stopping powers resulting from the adoption of two different sets of mean excitation energy values for water and graphite: (i) the currently ICRU recommended $I_w = 75$ eV and $I_g = 78$ eV and (ii) the recently proposed $I_w = 78$ eV and $I_g = 81.1$ eV. Twelve different ionization chamber models were studied. The Monte Carlo calculated $k_Q$ factors obtained in this chapter were compared to the experimental data obtained in chapters 4 and 5, as well as to other experimental data published in the literature.

6.1 Introduction

As discussed in section 1.2, due to a lack of an appropriate Monte Carlo code, no Monte Carlo calculations of beam quality correction factors in proton beams have been done so far using the approach of Sempau et al. (2004), i.e. using equation (2.47). Recently Salvat (2013) has developed \textsc{penh}, an extension of the \textsc{penelope} code that includes the transport of protons based on their electromagnetic interactions in matter. Proton nuclear interactions, however, have not been included. Sterpin et al. (2013) introduced proton nuclear interactions for six isotopes ($^1$H, $^{12}$C, $^{14}$N, $^{16}$O, $^{31}$P, $^{40}$Ca) in \textsc{penh}. However, the simulation of ionization chambers requires more than these six isotopes. Although not dominant, the effect of proton nuclear interactions cannot be neglected in proton therapy. Whereas the contribution of charged particles heavier than protons to the absorbed dose to water might, on a first approximation, be considered negligible (Paganetti 2002, Fippel &
Soukup 2004), the contribution of secondary protons (i.e. protons originating from inelastic nuclear interactions) cannot be disregarded, as they contribute roughly to 10% of the dose deposited by a proton beam in the clinical energy range (Paganetti 2002).

This chapter describes the calculation of beam quality correction factors for monoenergetic proton beams. The calculation is based on a detailed Monte Carlo simulation of ionization chambers in proton and $^{60}$Co gamma radiation beams, and the use of equation (2.47). $k_{Q,Q_0}$ factors were calculated for a wide range of plane-parallel ionization chambers and a limited set of cylindrical ionization chambers. Two different sets of mean exitation energy values for water ($I_w$) and graphite ($I_g$) were used: (i) the ICRU 37 and ICRU 49 values currently in use ($I_w = 75$ eV and $I_g = 78$ eV); and (ii) the latest $I$-values for water ($I_w = 78$ eV, Andreo et al. (2013)) and graphite ($I_g = 81.1$ eV, Burns et al. (2014)), to be recommended in a forthcoming ICRU report on key data for ionizing radiation dosimetry. Two different $W_{\text{air}}$ values for proton beams were also used accordingly (Andreo et al. 2013).

6.2 Materials and methods

We took $^{60}$Co gamma radiation as the reference beam quality $Q_0$ and monoenergetic proton beams of energies from 70 to 250 MeV as the user beam quality $Q$.

This section describes: (i) the Monte Carlo codes used in this chapter, (ii) the reference conditions used and the geometry of the simulations, (iii) the radiation sources, (iv) the transport simulation parameters, (v) the geometry of the simulated ionization chambers, and (vi) the $W_{\text{air},Q}$ values used.

6.2.1 Monte Carlo simulation codes

We used PEnH (Salvat 2013) for the calculation of beam quality correction factors in proton beams. PEnH is a Fortran subroutine package, which is linked to PEnELOPE (Salvat 2014), thus allowing for the simulation of coupled proton-electron-photon transport processes. As main program we used a version of PEnEASY (Sempau et al. 2011) that includes PEnH. As mentioned above, the only drawback of PEnH is that it does not include proton nuclear interactions and, therefore, it does not include the transport of secondary protons originating from inelastic nuclear interactions.

As the influence of secondary protons cannot be disregarded, we also used GAMOS to generate a realistic phase-space file (PSF) in water, just in front of the ionization chamber (see below). More specifically, we used GAMOSv4.1.0, which runs on GEANT4.9.6p02. We used the QGSP_BIC_EMY physics list (see section 3.2), together with the options: (i) $G4EmPenelopePhysics$
for the electromagnetic processes of photons, electrons and positrons, and (ii) \textit{G4UrbanMscModel96} for the multiple Coulomb scattering of electrons.

6.2.2 Reference conditions and geometry of the simulations

For the reference beam quality $^{60}\text{Co}$ we followed the reference conditions described in IAEA TRS-398. That is, we defined a $20 \times 20 \times 15 \text{cm}^3$ water phantom and we set the reference depth ($z_{\text{ref}}$) to 5 g cm$^{-2}$, the source-to-chamber distance (SCD) to 100 cm and the field size at the reference depth to $10 \times 10 \text{cm}^2$. For proton beams we also followed the reference conditions for monoenergetic proton beams described in IAEA TRS-398, but we set the reference depth to 2 g cm$^{-2}$, instead of 3 g cm$^{-2}$, as extensively discussed in chapter 4. To speed up the simulations of proton beams we used a water phantom of $20 \times 20 \times 5 \text{cm}^3$, since proton backscatter can be considered negligible—see e.g. Salvat (2013).

The absorbed dose to water at the reference depth was calculated as the average absorbed dose to water scored in a disc of 1 cm of radius and 250 \text{µm} of thickness centered at $z_{\text{ref}}$. This procedure introduced by Sempau et al. (2004) has become a common method to compute $D_w$ in $f_Q$ calculations, where the absorbed dose to water in a point is approximated by the average absorbed dose to water scored in a small volume. $D_{\text{air}}$ was calculated as the average absorbed dose to air in the ionization chamber sensitive volume. For both $^{60}\text{Co}$ and proton beams the ionization chambers were positioned as described in IAEA TRS-398, i.e. the reference point of the chamber was positioned on the central axis of the beam at the reference depth. For cylindrical chambers the reference point of the chamber is the center of the cavity volume; for plane-parallel chambers, it is on the inner surface of the entrance window at its center (see table 2.2). Chapters 4 and 5 questioned the IAEA TRS-398 recommendation of setting the reference point of cylindrical chambers at the reference depth for monoenergetic proton beams. This point will not be addressed in this chapter. Herein we focused on the calculation of $k_Q$ for plane-parallel chambers, which are not affected by this debate. We also simulated a limited set of cylindrical chambers, in order to validate our simulations with published experimental data.

6.2.3 Radiation sources

As $^{60}\text{Co}$-beam source we simulated a photon point source located 100 cm away from $z_{\text{ref}}$, shaping a $10 \times 10 \text{cm}^2$ field at $z_{\text{ref}}$. The energy of the photons emerging from the source was sampled from the spectrum of the \textit{Bureau International des Poids et Mesures} (BIPM) $^{60}\text{Co}$-source published by Burns (2003). As this spectrum had been scored at a distance of 90 cm from the source, we transported the photons through 90 cm of vacuum and 5 cm of air before reaching the water phantom.
As proton source we used a phase-space file generated with GAMOS. We simulated a planar $10 \times 10 \text{cm}^2$ proton beam impinging on the surface of a water phantom. The incident protons were monoenergetic, monodirectional and perpendicular to the water phantom surface. We scored a PSF at the depth of 15 mm in water, including only those particles that can transport, i.e. protons, electrons, positrons and photons. PSFs were generated for five different proton energies (70, 100, 150, 200 and 250 MeV) and they were subsequently used as input PSF sources in \textsc{penh}. Table 6.1 shows the equivalence between the initial energy of the proton beam and the range in water for different $I_w$-values. The continuous slowing down approximation range ($R_{\text{CSDA}}$), the practical range ($R_p$) and the residual range ($R_{\text{res}}$) are defined in 2.2. In table 6.1 the residual range is given for a reference depth of $z_{\text{ref}} = 2 \text{g cm}^2$.

It is important to point out that, in the calculation of the beam quality correction factors, we assumed that the contribution to $D_w$ from the secondary protons and heavier charged particles generated in the vicinity of the reference point of measurement is comparable to the contribution to $D_{\text{air}}$ from the secondary protons and heavier charged particles generated in the ionization chamber materials. Thus, this work assumes that these two contributions cancel out in the numerator of equation (2.47) and therefore have a negligible effect on the calculated $k_Q$ values. This assumption is, of course, an additional source of uncertainty in the final $k_Q$ factors.
6.2.4 Transport simulation parameters

GAMOS

In GAMOS we set the production cuts for photons, electrons and positrons to 2.5 \( \mu \)m and the absorption energies of photons to \( E_{\text{abs}}(\gamma) = 1 \text{ keV} \), electrons and positrons to \( E_{\text{abs}}(e^-) = E_{\text{abs}}(e^+) = 200 \text{ keV} \) and protons to \( E_{\text{abs}}(p) = 1 \text{ MeV} \). Finally we limited the maximum step size of charged particles, so that they interacted at least 20 times before reaching the PSF scoring plane.

PENH

The transport simulation parameters in PENH are the same as in PENELOPE and they are described in detail in Salvat (2014).

In this work all the simulations had the same structure: a scoring volume, a detailed simulation region (around the scoring volume) and a mixed (class II) simulation region (surrounding these two). The scoring volume was either the water cavity (assumed to be good representative of a point) or the ionization chamber sensitive volume. The detailed and mixed simulation volumes were defined arbitrarily, but conservatively, as follows. We transported all electrons with energy higher than 200 keV, as these electrons have a radiation yield in water larger than 0.1\%. Where the probability for a 200 keV electron of reaching the scoring volume was negligible, we set the absorption energy for electrons to \( E_{\text{abs}}(e^-) = 200 \text{ keV} \); where it was non-negligible, we set it to \( E_{\text{abs}}(e^-) = 1 \text{ keV} \). In water, for instance, we defined this probability based on the \( R_{\text{CSDA}} \) in water of a 200 keV electron, multiplied by a factor of 1.2—to account for the possibility that an electron may travel a distance beyond its \( R_{\text{CSDA}} \) due to energy-loss straggling (Sempau & Andreo 2006). In ionization chamber geometries the influence of the different materials was taken into account. Finally, we defined the detailed and mixed simulation volumes as the regions with \( E_{\text{abs}}(e^-) = 1 \text{ keV} \) and \( E_{\text{abs}}(e^-) = 200 \text{ keV} \), respectively.

Absorption energies for photons and protons were set to \( E_{\text{abs}}(\gamma) = 1 \text{ keV} \) and \( E_{\text{abs}}(p) = 1 \text{ MeV} \) for all regions. In the scoring volume and the detailed simulation region we used detailed simulation, i.e. we simulated every single interaction. Absorption energies for electrons and positrons were set to \( E_{\text{abs}}(e^-) = E_{\text{abs}}(e^+) = 1 \text{ keV} \) and all the transport simulation parameters \((C_1, C_2, W_{\text{cc}}, \text{ and } W_{\text{cr}})\) for all charged particles were set to zero. In the mixed simulation region the absorption energy for electrons and positrons was 200 keV. For all charged particles we used \( W_{\text{cc}} = 10 \text{ keV} \) and \( W_{\text{cr}} = 1 \text{ keV} \) and we increased gradually \( C_1 \) and \( C_2 \) from 0.05 (everywhere in the mixed simulation region within a distance less than or equal to 5 mm from the scoring volume) to 0.1 (elsewhere). In the mixed simulation region we also set \( ds_{\text{max}} \) in such a way that each charged particle interacted at least 20 times in each body.
Chapter 6. Monte Carlo calculation of $k_Q$ factors

Table 6.2: Dimensions and material composition of the plane-parallel ionization chambers simulated in this work.

<table>
<thead>
<tr>
<th>Ionization chamber model</th>
<th>Entrance window thickness</th>
<th>Electrode spacing</th>
<th>Collecting electrode thickness</th>
<th>Sensitive volume radius</th>
<th>Guard ring width</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exradin A10</td>
<td>0.99 mm PMMA 0.10 mm air 25 $\mu$m kapton</td>
<td>2.01 mm</td>
<td>0.38 mm C552</td>
<td>2.85 mm</td>
<td>4.1 mm</td>
</tr>
<tr>
<td>Exradin A11</td>
<td>0.99 mm C552 0.10 mm air 25 $\mu$m kapton</td>
<td>2.01 mm</td>
<td>0.51 mm C552</td>
<td>9.93 mm</td>
<td>4.4 mm</td>
</tr>
<tr>
<td>Exradin A11TW</td>
<td>0.99 mm PMMA 0.10 mm air 25 $\mu$m kapton</td>
<td>3 mm</td>
<td>0.51 mm C552</td>
<td>9.93 mm</td>
<td>2.8–4.4 mm</td>
</tr>
<tr>
<td>IBA NACP-02</td>
<td>0.1 mm mylar 0.5 mm graphite ($\rho_g = 1.82$ g cm$^{-3}$)</td>
<td>2 mm</td>
<td>50 $\mu$m graphite ($\rho_g = 0.93$ g cm$^{-3}$) 0.25 mm rexolite</td>
<td>5 mm</td>
<td>3.25 mm</td>
</tr>
<tr>
<td>IBA PPC-05</td>
<td>1 mm C552 0.6 mm</td>
<td></td>
<td>0.1 mm graphite ($\rho_g = 1.7$ g cm$^{-3}$) 0.5 mm PEEK</td>
<td>4.95 mm</td>
<td>3.95 mm</td>
</tr>
<tr>
<td>IBA PPC-40</td>
<td>0.9 mm PMMA 0.1 mm graphite ($\rho_g = 0.93$ g cm$^{-3}$)</td>
<td>2 mm</td>
<td>0.1 mm graphite ($\rho_g = 0.93$ g cm$^{-3}$)</td>
<td>8 mm</td>
<td>4.0 mm</td>
</tr>
<tr>
<td>PTW Advanced Markus</td>
<td>0.87 mm PMMA 0.4 mm air 30 $\mu$m polyethylene</td>
<td>1 mm</td>
<td>20 $\mu$m graphite ($\rho_g = 0.82$ g cm$^{-3}$)</td>
<td>2.5 mm</td>
<td>2 mm</td>
</tr>
<tr>
<td>PTW Markus</td>
<td>0.87 mm PMMA 0.4 mm air 30 $\mu$m polyethylene</td>
<td>2 mm</td>
<td>20 $\mu$m graphite ($\rho_g = 0.82$ g cm$^{-3}$)</td>
<td>2.65 mm</td>
<td>0.25 mm</td>
</tr>
<tr>
<td>PTW Roos</td>
<td>1.1 mm PMMA 20 $\mu$m graphite ($\rho_g = 0.82$ g cm$^{-3}$)</td>
<td>2 mm</td>
<td>20 $\mu$m graphite ($\rho_g = 0.82$ g cm$^{-3}$)</td>
<td>7.5 mm</td>
<td>4 mm</td>
</tr>
</tbody>
</table>

To reduce the statistical uncertainty, we also applied the variance reduction technique of particle splitting to all the particles reaching the scoring volume (with a splitting factor of 10). We implemented particle splitting in such a way that split particles could not be split again.

6.2.5 Ionization chambers

As mentioned above, this work focuses on the simulation of plane-parallel ionization chambers. We simulated accurately the geometry of nine different chambers: the Exradin A10, A11 and A11TW (Standard Imaging, Middleton WI, USA); the IBA NACP-02, PPC-05 and PPC-40; and the PTW Advanced Markus (Type 34045), Markus (Type 23343) and Roos (Type 34001). For the Exradin and IBA plane-parallel chambers very detailed descriptions of the geometry and materials of the chambers were provided by the manufacturers. For the Exradin chambers geometry files were built from the blueprints; for the IBA chambers we adapted the geometry files prepared by
Sempau et al. (2004). For the PTW chambers a less detailed description of the geometry and partial information of the materials of the chambers were also provided by the manufacturer. It is well-known that small variations in the dimensions and material composition of the detection volume and surrounding bodies (entrance window, collecting electrode, guard ring, etc.) have a significant effect on $D_{\text{air}}$. Table 6.2 summarizes the dimensions and material composition of the plane-parallel ionization chambers simulated in this work.

In addition to plane-parallel chambers, we also simulated three different models of cylindrical chambers: IBA FC65-G, IBA FC65-P and NE 2571. As mentioned above, we simulated this limited set of cylindrical chambers in order to validate our calculations with the few experimental data available in the literature (Palmans et al. 2001, 2002, Medin et al. 2006, Medin 2010) and the results of chapters 4 and 5. The geometry and materials of these chambers were taken from manufacturer information (drawings and technical specifications) available online. For the NE 2571 we simulated the geometry using the description and materials of Nuclear Enterprises (1984) and additional information taken from Aird & Farmer (1972) and Wulff et al. (2008). Based on Nuclear Enterprises (1984), we assumed the insulator material to be polychlorotrifluoroethylene (PCTFE), instead of polytetrafluoroethylene (PTFE) assumed by other authors (Wulff et al. 2008, Erazo & Lallena 2013). Also, as the NE 2571 is non-waterproof, we simulated a 0.5 mm PMMA sleeve around the chamber.

6.2.6 $W_{\text{air}}$ value for proton beams

As pointed out by Andreo et al. (2013)—where new $I_w$ and $I_g$ values were presented along with their impact on air kerma and absorbed dose to water standards—for proton beam dosimetry a change in $I$-values may also require a change in $W_{\text{air},Q}$. In this work, in order to calculate the beam quality correction factors for proton beams using equation (2.47), we are interested in the ratio between $W_{\text{air},Q}$ and $W_{\text{air},Q_0}$. When using ICRU 37 and ICRU 49 $I$-values, we used the currently recommended $W_{\text{air}}$ values ($W_{\text{air},Q_0} = 33.97 \text{ eV}$, $W_{\text{air},Q} = 34.23 \text{ eV}$) (Andreo et al. 2000, Jones et al. 2007), so that $W_{\text{air},Q}/W_{\text{air},Q_0} = 1.008(4)$. According to Andreo et al. (2013), the adoption of $I_w = 78 \text{ eV}$ and $I_g = 81.1 \text{ eV}$ should be accompanied with an increase in $W_{\text{air},Q}$ of about 0.6% (i.e. $W_{\text{air},Q} = 34.44 \text{ eV}$), under the assumption of no changes in $p_Q$, while $W_{\text{air},Q_0}$ remains unchanged. Thus, when using these new $I$-values, we used $W_{\text{air},Q}/W_{\text{air},Q_0} = 1.014(4)$. 
Table 6.3: Monte Carlo calculated $f_{Q_0}$ factors (i.e. for $^{60}$Co gamma radiation) for different plane-parallel ionization chambers and comparison with values in the literature. The values within parenthesis correspond to one standard uncertainty in the last digits.

<table>
<thead>
<tr>
<th>Ionization chamber model</th>
<th>$I_w = 78$ eV</th>
<th>$I_w = 75$ eV</th>
<th>$I_g = 81.1$ eV</th>
<th>$I_g = 78$ eV</th>
</tr>
</thead>
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<td><strong>Exradin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A10</td>
<td>1.1225(20)</td>
<td>1.1249(20)</td>
<td>1.0951(5)</td>
<td>1.1088(26)</td>
</tr>
<tr>
<td>A11</td>
<td>1.1071(15)</td>
<td>1.1087(15)</td>
<td>1.1158(5)</td>
<td>1.1124(16)</td>
</tr>
<tr>
<td>A11TW</td>
<td>1.0979(14)</td>
<td>1.1016(14)</td>
<td>1.1079(14)</td>
<td>1.1055(16)</td>
</tr>
<tr>
<td><strong>IBA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NACP-02</td>
<td>1.1523(15)</td>
<td>1.1536(15)</td>
<td>1.1578(7)</td>
<td>1.1562(4)</td>
</tr>
<tr>
<td>PPC-05</td>
<td>1.1374(18)</td>
<td>1.1381(18)</td>
<td>1.1410(10)</td>
<td>1.1475(5)</td>
</tr>
<tr>
<td>PPC-40</td>
<td>1.1403(12)</td>
<td>1.1468(12)</td>
<td>1.1455(7)</td>
<td>1.1440(5)</td>
</tr>
<tr>
<td><strong>PTW</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adv. Markus</td>
<td>1.1470(23)</td>
<td>1.1464(23)</td>
<td>1.1466(5)</td>
<td>1.1478(6)</td>
</tr>
<tr>
<td>Markus</td>
<td>1.1434(18)</td>
<td>1.1456(18)</td>
<td>1.1416(4)</td>
<td>1.1467(7)</td>
</tr>
<tr>
<td>Roos</td>
<td>1.1406(12)</td>
<td>1.1459(12)</td>
<td>1.1485(5)</td>
<td>1.1509(5)</td>
</tr>
</tbody>
</table>

Table 6.4: Monte Carlo calculated $f_{Q_0}$ factors (i.e. for $^{60}$Co gamma radiation) for cylindrical ionization chambers and comparison with values in the literature. The values within parenthesis correspond to one standard uncertainty in the last digit.

<table>
<thead>
<tr>
<th>Ionization chamber model</th>
<th>$I_w = 75$ eV; $I_g = 78$ eV</th>
<th>$I_w = 78$ eV; $I_g = 81.1$ eV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IBA FC65-G</strong></td>
<td>1.1123(9)</td>
<td>1.1050(9)</td>
</tr>
<tr>
<td><strong>IBA FC65-P</strong></td>
<td>1.1169(9)</td>
<td>1.1145(9)</td>
</tr>
<tr>
<td><strong>NE 2571</strong></td>
<td>1.1111(9)</td>
<td>1.1039(9)</td>
</tr>
</tbody>
</table>

6.3 Results and discussion

6.3.1 $^{60}$Co beam quality

Table 6.3 and table 6.4 show the Monte Carlo calculated $f_{Q_0}$ factors (i.e. for $^{60}$Co gamma radiation) for the different plane-parallel and cylindrical ionization chambers studied in this work. We calculated the $f_{Q_0}$ factors using the electronic stopping powers resulting from the adoption of two different sets of $I$-values for water and graphite: the ICRU $I$-values ($I_w = 75$ eV; $I_g = 78$ eV) and the new $I$-values proposed by Andreo et al. (2013) and Burns et al. (2014) ($I_w = 78$ eV; $I_g = 81.1$ eV).

Table 6.3 also shows other $f_{Q_0}$ factors published in the literature for the same plane-parallel ionization chambers and calculated using the ICRU $I$-values. Panettieri et al. (2008) calculated the $f_{Q_0}$ factor for the three IBA...
plane-parallel chambers studied in this work with penelope-2006. The authors used three different $^{60}$Co sources (a monoenergetic beam, a photon spectrum and a phase-space file). The values shown in table 6.3 are the $f_{Q_0}$ factors reported as the weighted mean of the values obtained with the three different $^{60}$Co sources.

Muir et al. (2012) calculated $k_Q$ factors in megavoltage photon beams for most of the ionization chambers studied in this work with egsnrc. Although the explicit $f_{Q_0}$ factors were not reported in their work, the values in table 6.3 were provided by the authors in a private communication. For the NACP-02 $f_{Q_0}$ factor, table 6.3 shows the value corresponding to the geometry studied in this work (0.6 mm-thick entrance window, $\rho_g = 1.82 \text{ g cm}^{-3}$), also provided by the authors.

Zink & Wulff (2012) calculated the perturbation correction factors $p_{Q_0}$ for the NACP-02 and the three PTW chambers studied in this work with egsnrc. The values shown in table 6.3 are the product of the reported $p_{Q_0}$ factors and the IAEA TRS-398 water/air stopping power ratio for $^{60}$Co gamma radiation, $s_{w,\text{air},Q_0} = 1.133$. The uncertainty values shown in table 6.3 correspond to the uncertainty estimates given by these authors for the $p_{Q_0}$ factors—i.e. they do not take the uncertainty of $s_{w,\text{air},Q_0}$ into account. Again, for the NACP-02 $f_{Q_0}$ factor we took the value corresponding to the geometry studied in this work.

Finally Erazo et al. (2014) calculated $k_{Q,Q_0}$ factors for electron beams for the NACP-02 and the three Exradin ionization chambers studied in this work with penelope-2011. Although the explicit $f_{Q_0}$ factors were not reported in their work, the values in table 6.3 were also provided by the authors in a private communication.

Table 6.4 also shows $f_{Q_0}$ factors for cylindrical chambers published in the literature. Muir & Rogers (2010) calculated $k_Q$ factors in megavoltage photon beams for the three cylindrical chambers studied in this work with egsnrc and using ICRU I-values. Although the explicit $f_{Q_0}$ factors were not reported in their work, the values in table 6.4 were provided by the authors in a private communication. Andreo et al. (2013) calculated the $f_{Q_0}$ factor of the NE 2571 for the same two sets of I-values studied in this work, also with egsnrc.

For the plane-parallel ionization chambers studied in this work we found that the adoption of new I-values leads to a decrease in $f_{Q_0}$ of around 0.2%, ranging from no changes (PTW Adv. Markus) to a decrease of about 0.6% (IBAPPC-40). It should be noticed that the estimate of Andreo et al. (2013) for the decrease in $s_{w,\text{air},Q_0}$ (resulting from the adoption of new I-values) was 0.6%. Hence, the new I-values cause an increase in the perturbation correction factors for $^{60}$Co estimated to be negligible for the IBA PPC-40 chamber and up to 0.6% for the PTW Adv. Markus, where the changes in $s_{w,\text{air},Q_0}$ and $p_{Q_0}$ practically cancel each other.

For cylindrical chambers the adoption of new I-values results in a de-
crease in $f_{Q_0}$ of 0.2% for the IBA FC65-P and of about 0.7% for the graphite-walled chambers (IBA FC65-G and NE 2571). Thus, for graphite-walled cylindrical chambers, the new $I$-values result in negligible changes in $p_{Q_0}$, which is consistent with the 0.2% increase estimated by Andreo et al. (2013) for the NE 2571.

The vast majority of $f_{Q_0}$ factors calculated in this work using ICRU $I$-values agree with those published in the literature calculated, using the same $I$-values, within 0.5%—which are differences consistent with the use of different Monte Carlo codes. In what follows, we will limit the discussion of the results to those differences larger than 0.5%.

For the Exradin A10 our $f_{Q_0}$ factor differs by 1.5% and 2.7% from the values of Erazo et al. (2014) and Muir et al. (2012), respectively. Such large differences are only observed with this ionization chamber model. In addition to the Monte Carlo code (or its version) and the $^{60}$Co spectrum used, there are two important differences between our simulations and those by these authors: (i) for the description of the geometry we used an updated version of the A10 blueprints provided by the manufacturer, fixing a ‘bug’ in the vicinity of the chamber sensitive volume; and (ii) the transport simulation parameters used in the chamber sensitive volume and surrounding bodies were rather different. Whereas our work used detailed simulation (i.e. all collisions were simulated), these authors used a mixed simulation scheme. The smaller the air cavity, the larger the influence of transport simulation parameters. This explains the larger effect on the A10 chamber, which has a small sensitive volume (see table 6.2).

The $f_{Q_0}$ factor of the NACP-02 chamber agrees within 0.2%, 0.2% and 0.4% with the values of Muir et al. (2012), Erazo et al. (2014) and Panettieri et al. (2008), respectively, but differs by 0.7% from the value of Zink & Wulff (2012). This discrepancy could be explained in terms of the different material composition of the collecting electrode used by Zink & Wulff (2012), which may affect $f_{Q_0}$ by up to 0.5% (Muir et al. 2012).

For the IBA PPC-05 our $f_{Q_0}$ factor agrees within 0.3% with the value of Panettieri et al. (2008), but it differs by 0.8% from the value of Muir et al. (2012). As in the case of the Exradin A10 chamber, this discrepancy could arise from the difference between detailed and mixed simulation—which, as mentioned above, is more notorious for small volume ionization chambers like the IBA PPC-05 (see table 6.2).

### 6.3.2 Proton beam qualities

Table 6.5 shows the Monte Carlo calculated beam quality correction factors in monoenergetic proton beams for all the ionization chambers studied in this work, at a reference depth of $2 \text{ g cm}^{-2}$, as a function of the initial energy of the beam. The uncertainty estimate shown is the combined standard uncertainty of $f_Q$ (type A), $f_{Q_0}$ (type A) and $W_{\text{air},Q}/W_{\text{air},Q_0}$ (type B). Note
### 6.3. Results and discussion

Table 6.5: Monte Carlo calculated $k_Q$ factors for monoenergetic proton beams, at the reference depth of 2 g cm$^{-2}$, as a function of the initial proton energy. The values within parenthesis correspond to one standard uncertainty in the last digit.

$I_w = 75$ eV; $I_g = 78$ eV; $W_{air,Q}/W_{air,Q_0} = 1.008$

<table>
<thead>
<tr>
<th>IC model</th>
<th>70</th>
<th>100</th>
<th>150</th>
<th>200</th>
<th>250</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exradin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A10</td>
<td>1.012(6)</td>
<td>1.019(6)</td>
<td>1.007(6)</td>
<td>1.020(6)</td>
<td>1.013(6)</td>
</tr>
<tr>
<td>A11</td>
<td>1.012(6)</td>
<td>1.023(5)</td>
<td>1.022(5)</td>
<td>1.025(5)</td>
<td>1.022(6)</td>
</tr>
<tr>
<td>A11TW</td>
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<td>1.030(5)</td>
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<td>1.029(6)</td>
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<td></td>
</tr>
<tr>
<td>NACP-02</td>
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<td>0.987(5)</td>
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<td>0.990(5)</td>
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<td>0.999(5)</td>
<td>1.001(5)</td>
<td>1.004(6)</td>
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<td>0.991(5)</td>
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<td>0.993(5)</td>
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<td>PTW</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adv. Markus</td>
<td>1.007(6)</td>
<td>1.002(6)</td>
<td>0.991(6)</td>
<td>1.000(7)</td>
<td>0.995(7)</td>
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<tr>
<td>Markus</td>
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<td>1.000(6)</td>
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<td>0.993(5)</td>
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<td>0.994(5)</td>
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<td></td>
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</tr>
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<td>FC65-G</td>
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<td>1.036(5)</td>
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<tr>
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<td>1.064(5)</td>
<td>1.037(5)</td>
<td>1.022(5)</td>
<td>1.022(5)</td>
<td>1.024(5)</td>
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</table>

$I_w = 78$ eV; $I_g = 81.1$ eV; $W_{air,Q}/W_{air,Q_0} = 1.014$

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<tr>
<th>IC model</th>
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<td></td>
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<td>A10</td>
<td>1.013(6)</td>
<td>1.013(6)</td>
<td>1.023(6)</td>
<td>1.021(6)</td>
<td>1.021(6)</td>
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<td>1.014(5)</td>
<td>1.026(5)</td>
<td>1.023(5)</td>
<td>1.025(5)</td>
<td>1.028(6)</td>
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<td>1.034(6)</td>
<td>1.039(5)</td>
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<td>1.038(6)</td>
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<td></td>
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</tr>
<tr>
<td>NACP-02</td>
<td>0.981(5)</td>
<td>0.987(5)</td>
<td>0.987(5)</td>
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<td>PPC-05</td>
<td>0.990(5)</td>
<td>1.003(5)</td>
<td>1.007(5)</td>
<td>1.003(5)</td>
<td>1.004(6)</td>
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<tr>
<td>PPC-40</td>
<td>0.992(5)</td>
<td>0.996(5)</td>
<td>0.998(5)</td>
<td>0.996(5)</td>
<td>0.997(5)</td>
</tr>
<tr>
<td>PTW</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Adv. Markus</td>
<td>1.001(6)</td>
<td>0.997(6)</td>
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<td>1.006(7)</td>
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<td>Markus</td>
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<td>1.012(6)</td>
<td>1.008(6)</td>
<td>1.007(6)</td>
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<td>0.993(5)</td>
<td>0.994(5)</td>
<td>0.998(5)</td>
<td>0.999(5)</td>
<td>0.999(5)</td>
</tr>
<tr>
<td>IBA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FC65-G</td>
<td>1.067(5)</td>
<td>1.040(5)</td>
<td>1.031(5)</td>
<td>1.025(5)</td>
<td>1.020(5)</td>
</tr>
<tr>
<td>FC65-P</td>
<td>1.065(5)</td>
<td>1.039(5)</td>
<td>1.029(5)</td>
<td>1.025(5)</td>
<td>1.022(5)</td>
</tr>
<tr>
<td>NE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2571</td>
<td>1.069(5)</td>
<td>1.043(5)</td>
<td>1.032(5)</td>
<td>1.027(5)</td>
<td>1.023(5)</td>
</tr>
</tbody>
</table>
Figure 6.1: Comparison of the Monte Carlo $k_Q$ factors for cylindrical ionization chambers calculated in this work and the IAEA TRS-398 $k_Q$ factors (solid line), calculated using ICRU $I$-values, as a function of $R_{\text{res}}$. The uncertainty bars and the dashed lines correspond to one standard uncertainty in the data points and the IAEA TRS-398 values, respectively.
Figure 6.2: Comparison of the Monte Carlo $k_Q$ factors for plane-parallel ionization chambers calculated in this work and the IAEA TRS-398 $k_Q$ factors (solid line), calculated using ICRU $I$-values, as a function of $R_{res}$. The uncertainty bars and the dashed lines correspond to one standard uncertainty in the data points and the IAEA TRS-398 values, respectively.
that \( f_Q \) factors may be obtained by simply dividing the \( k_Q \) factors by the \( W_{\text{air}} \) ratio and the corresponding \( f_{Q_0} \) factor in table 6.3 (or table 6.4).

From the values in table 6.5 it can be seen that the adoption of new \( I \)-values results in an average increase in \( k_Q \) of about 0.3%—changes in \( k_Q \) factors are, however, strongly dependent on the ionization chamber model. For plane-parallel chambers, changes in \( k_Q \) range from -0.6% up to 1.6%; for cylindrical chambers, they range from -0.1% to 1%. For the NE 2571 we obtained an average increase in \( k_Q \) of about 0.5%, which agrees within one standard uncertainty with the estimate of Andreo et al. (2013) of no changes (based on the assumption of negligible perturbation effects).

Figure 6.1 and figure 6.2 show a comparison between the \( k_Q \) factors of some of the ionization chambers studied in this work (calculated with the two sets of \( I \)-values) and the \( k_Q \) factors tabulated in IAEA TRS-398 (calculated using ICRU \( I \)-values), as a function of the residual range—see table 6.1 for energy-range equivalence. Figure 6.1 shows the \( k_Q \) factors for cylindrical ionization chambers and it includes the experimental values of Medin et al. (2006) and Medin (2010), determined with water calorimetry. Figure 6.2 shows the \( k_Q \) factors for plane-parallel chambers.

All the \( k_Q \) factors calculated in this work using ICRU \( I \)-values agree within 2.3% or better with the \( k_Q \) factors tabulated in IAEA TRS-398 and within 1% or better with the experimental values of Medin et al. (2006) and Medin (2010). The \( k_Q \) factors calculated using \( I_w = 78 \text{ eV} \) and \( I_g = 81.1 \text{ eV} \) also agree within 1.1% or better with the experimental values. Despite this agreement, the dependence of our \( k_Q \) factors with the residual range shows a different trend than IAEA TRS-398 values.

For cylindrical chambers, figure 6.1 shows that the variation of our \( k_Q \) factors with the residual range is of the order of 5% (within a \( R_{\text{res}} \) range from 2 to 37 g cm\(^{-2}\)), much larger than that of IAEA TRS-398 values (smaller than 0.5%). Such a variation is mainly due to the increase of our \( k_Q \) factors at small residual ranges, which, in turn, is due to the fact that the reference point of the chamber—and not its effective point of measurement—is positioned at the reference measurement depth, as extensively discussed in chapters 4 and 5.

For plane-parallel ionization chambers, figure 6.2 shows that the agreement between our \( k_Q \) factors and IAEA TRS-398 values is better (almost always within 1%) than for cylindrical ionization chambers. However, the variation of the \( k_Q \) factors with the residual range seems to follow a different trend. Whereas IAEA TRS-398 \( k_Q \) factors decrease slightly with increasing residual range, our \( k_Q \) factors seem to slightly increase with increasing residual range.

Excluding the case of cylindrical chambers at small residual ranges (because of the reasons mentioned above), all our \( k_Q \) factors calculated using ICRU \( I \)-values agree with the IAEA TRS-398 values within the standard uncertainty stated in the Code of Practice. Compatible with this agreement
6.3. Results and discussion

Table 6.6: Ratio of $k_Q$ factors, at the reference depth of $2 \text{ g cm}^{-2}$, of different ionization chambers studied in this chapter and comparison with experimental values in the literature. The values within parenthesis correspond to one standard uncertainty in the last digit.

<table>
<thead>
<tr>
<th>Ionization chamber</th>
<th>$I_w = 75 \text{ eV}$</th>
<th>$I_w = 78 \text{ eV}$</th>
<th>Palmans et al.</th>
<th>Palmans et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBA FC65-G/NE 2571</td>
<td>1.001(2)</td>
<td>0.998(2)</td>
<td>0.997(2)</td>
<td></td>
</tr>
<tr>
<td>IBA NACP-02/NE 2571</td>
<td>0.923(3)</td>
<td>0.917(3)</td>
<td>0.930(3)</td>
<td></td>
</tr>
<tr>
<td>PTW Markus/NE 2571</td>
<td>0.943(4)</td>
<td>0.938(4)</td>
<td>0.940(3)</td>
<td></td>
</tr>
<tr>
<td>PTW Roos/NE 2571</td>
<td>0.932(2)</td>
<td>0.929(2)</td>
<td>0.937(3)</td>
<td></td>
</tr>
</tbody>
</table>

$R_{res} \sim 2.5 \text{ g cm}^{-2}$

<table>
<thead>
<tr>
<th>Ionization chamber</th>
<th>$I_w = 75 \text{ eV}$</th>
<th>$I_w = 78 \text{ eV}$</th>
<th>Chapter 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBA NACP-02/IBA FC65-G</td>
<td>0.954(3)</td>
<td>0.948(3)</td>
<td></td>
</tr>
<tr>
<td>PTW Adv. Markus/IBA FC65-G</td>
<td>0.967(5)</td>
<td>0.958(5)</td>
<td></td>
</tr>
<tr>
<td>PTW Markus/IBA FC65-G</td>
<td>0.971(4)</td>
<td>0.963(4)</td>
<td></td>
</tr>
<tr>
<td>PTW Roos/IBA FC65-G</td>
<td>0.958(2)</td>
<td>0.955(2)</td>
<td></td>
</tr>
</tbody>
</table>

$R_{res} \sim 6 \text{ g cm}^{-2}$

is the fact that our mean $k_Q$ values and IAEA TRS-398 mean values may differ by up to 1.8% for some ionization chamber models. Furthermore, these differences (between mean $k_Q$ values) are strongly dependent on the ionization chamber model and the proton beam quality. Such a dependence seems to indicate that perturbation correction factors in proton beams could be significantly different from unity, at least for the some of the ionization chambers studied in this work. For graphite-walled Farmer chambers, for instance, we found that for $R_{res} > 14 \text{ g cm}^{-2}$ the differences between our mean $k_Q$ values and IAEA TRS-398 values are of about 1.7%. Part of these differences (0.8–0.9%) arise from a higher $f_{Q0}$ factor ($f_{Q0} = 1.111–1.112$) than that in IAEA TRS-398 ($f_{Q0} = 1.102$). The remaining part arise from a smaller $f_Q$ factor, pointing at $p_Q \sim 0.992(2)$, slightly lower than the value calculated by Palmans (2011) ($p_Q = 0.9965$). Note that these differences (for graphite-walled Farmer chambers) bring the comparison between reference dosimetry and Faraday dosimetry in chapter 4 in much better agreement—from 3% to approximately 1.5%.

To further validate the Monte Carlo $k_Q$ factors calculated in this work,
table 6.6 compares the ratio of $k_Q$ factors ($k_Q/k_{Q}^{\text{ref}}$) for some of the ionization chambers studied in this work with experimental data published in the literature. Note that the $k_Q$ ratio of two ionization chambers has the advantage that it does not depend on the adoption of specific $W_{\text{air}}$ values. Palmans et al. (2001) and Palmans et al. (2002) determined experimentally the ratio of $k_Q$ factors between different ionization chambers and the NE 2571 chamber (as reference chamber), for a non-modulated proton beam of $R_{\text{res}} = 2.65$ cm. In their work, the authors reported $p_Q$ ratios (instead of $k_Q$ ratios), after applying a series of theoretical corrections to the experimental data. Herein, we reverted these corrections, so that table 6.6 shows the experimental $k_Q$ ratios obtained by these authors. Also in chapter 5 we determined the ratio of $k_Q$ factors for different ionization chambers in a proton beam of $R_{\text{res}} \simeq 6$ cm. The values shown in table 6.6 correspond to the results reported for the pseudo-monoenergetic proton beam. Note that here the IBA FC65-G is taken as reference chamber, instead of the PTW Markus. The reason for that is the lower quality of the geometry description of PTW chambers (see section 6.2.5).

The $k_Q$ ratios calculated in this work using ICRU $I$-values were found to agree within 0.4%, 0.7% and 1.9%, or better, with the experimental values of Palmans et al. (2001), Palmans et al. (2002) and chapter 5, respectively. The $k_Q$ ratios calculated using $I_w = 78$ eV and $I_g = 81.1$ eV were found to agree within 0.6%, 1.3% and 1.0%, or better, with the experimental values of Palmans et al. (2001), Palmans et al. (2002) and chapter 5, respectively.

It is worth mentioning again that the $k_Q$ factors calculated in this chapter are based on the assumption that the contribution to the absorbed dose to water at the reference depth from the secondary protons and heavier charged particles generated in the vicinity of $z_{\text{ref}}$ is comparable to the contribution to the absorbed dose to air in the ionization chamber sensitive volume from the secondary protons and heavier charged particles generated in the ionization chamber materials. Despite this assumption, we found a good agreement between our Monte Carlo calculated $k_Q$ factors and the experimental data published in the literature.

Finally, it is important to point out that the $k_Q$ factors calculated in this work include inherently a correction for dose gradient effects in monoenergetic proton beams. Therefore, they should not be used in modulated proton beams, where dose gradients are much smaller.

## 6.4 Conclusions

This chapter calculated $f_{Q0}$ factors (in $^{60}$Co gamma radiation) and $k_Q$ factors in monoenergetic proton beams for a wide range of ionization chambers, based on Monte Carlo simulation. We used the electronic stopping powers resulting from the adoption of two different sets of $I$-values for water and
graphite: ICRU $I$-values ($I_w = 75\text{ eV}; I_g = 78\text{ eV}$) and new $I$-values proposed by Andreo et al. (2013) and Burns et al. (2014) ($I_w = 78\text{ eV}; I_g = 81.1\text{ eV}$). The $f_{Q0}$ factors calculated in this work were in good agreement with both Monte Carlo calculated and experimental values published in the literature. Except for the case of cylindrical chambers at small residual ranges, our Monte Carlo calculated $k_Q$ factors agreed with the values tabulated in IAEA TRS-398 and the experimental values in the literature within their stated standard uncertainties. The results of this work point at perturbation correction factors in proton beams that may differ significantly from unity for some of the ionization chambers studied. Nevertheless, an independent calculation of $k_Q$ factors in proton beams—by other authors and, ideally, with a different Monte Carlo code—would be of interest for the scientific community in order to validate, or question, the $k_Q$ factors reported here.
Chapter 7

Reference dosimetry of proton pencil beams based on dose-area product: a proof of concept

This chapter describes a novel approach to the reference dosimetry of proton pencil beams based on the concept of dose-area product. The dose-area product is the integral of the absorbed dose to water over the plane perpendicular to the beam direction. For proton pencil beams, the dose-area product is a quantity easier to determine than the absorbed dose to water at a point. In this chapter, we compare the reference dosimetry of proton pencil beams based on dose-area product with the standard approach based on the IAEA TRS-398 Code of Practice.

7.1 Introduction

IAEA TRS-398 recommends the determination of the absorbed dose to water in the centre of a broad field (10 × 10 cm²) with a ‘point-like’ ionization chamber—see table 2.2. In proton (and heavier charged-particle) pencil beam delivery systems, a broad field can be delivered by scanning the narrow pencil beam laterally, i.e. across the plane perpendicular to the beam direction. This way of producing a broad field has nevertheless one main drawback: it is very sensitive to delivery errors—in particular, to beam position errors. That is, small errors in beam position during the delivery of the field might have a significant effect on $D_w$ at the reference point of measurement (i.e. at the centre of the field). A more natural, and more robust, approach to the reference dosimetry of narrow pencil beams is the determination of the dose-area product ($D_w A$) with a large-diameter ionization
The dose-area product, also called integral dose by Pedroni et al. (2005), is the integral of $D_w$ over the plane perpendicular to the beam direction. That is, instead of determining $D_w$ at the centre of a broad field with a small detector, to determine $D_w A$ of a small field with a large detector. These two approaches are reciprocal (Attix 1986) and therefore equivalent, as it will be shown below in section 7.2.

The dose-area product is a dosimetric quantity extensively used in diagnostic radiology (Alm-Carlsson et al. 2007). In particle therapy, it is typically used to express the integrated depth-dose curve of proton (or heavier charged-particle) pencil beams (Jones et al. 2007). The use of $D_w A$ in the dosimetry of small radiotherapy beams was first proposed by Djouguela et al. (2006) for narrow photon beams and it was later used by Gillin et al. (2010) to calibrate the beam monitor chamber of a spot-scanning proton beam delivery system. In both cases, the authors cross-calibrated a large-diameter ionization chamber against a reference cylindrical ionization chamber in a broad field. Gillin et al. (2010) also seem to assume a constant beam quality correction factor ($k_{Q,Q_{cross}}$) for all the measured proton beam qualities.

In this chapter, we based on IAEA TRS-398 formalism to investigate the reference dosimetry of proton pencil beams based on $D_w A$. First, we calibrated a large-diameter ionization chamber in terms of $D_w A$ in a $^{60}$Co beam. Second, we calculated the beam quality correction factor of the large-diameter ionization chamber in proton beams in a similar way as in chapter 6. Last, we compared the dose-area product approach to the standard ‘broad field–small detector’ approach. The advantage of pencil beam scanning delivery systems is that they are capable of delivering a homogeneous broad field by the superposition of narrow fields, which establishes an analytical relationship between the broad and narrow field dosimetry, as it is shown below. Thus, proton (or heavier charged particles) pencil beam scanning delivery systems are the ideal delivery systems to test the novel approach to reference dosimetry described in this chapter.

### 7.2 Theory

In this section, we will derive the relationship between (i) the dose-area product or integrated dose ($D_w A$) of a proton pencil beam of lateral Gaussian shape and (ii) the point dose ($D_w$) at the centre of a uniform field generated by the superposition of an infinite number of equally-spaced proton pencil beams.

To begin with, let us define $D(x, y, z)$ as the absorbed dose to water at a point $(x, y, z)$ in space delivered by a given radiation field. If the $z$-axis defines the beam direction, the integrated dose, $D(z)$, is defined as the
7.2. Theory

integral of \( D(x, y, z) \) over the plane perpendicular to the beam direction

\[
D(z) = \int_{-\infty}^{+\infty} \int_{-\infty}^{+\infty} D(x, y, z) \, dx \, dy. \tag{7.1}
\]

When the radiation field is a single proton pencil beam of lateral Gaussian shape travelling along \( z \) and centered at \((x_0, y_0)\),

\[
D(x, y, z) = D(x_0, y_0, z) \exp \left( -\frac{(x-x_0)^2}{2\sigma_x^2} \right) \exp \left( -\frac{(y-y_0)^2}{2\sigma_y^2} \right), \tag{7.2}
\]

where \( D(x_0, y_0, z) \) is the dose at the centre of the pencil as a function of \( z \); and \( \sigma_x \) and \( \sigma_y \) are the standard deviation of the Gaussian function in the directions \( x \) and \( y \), respectively. \( \sigma_x \) and \( \sigma_y \) are also a function of \( z \), but this dependency is omitted in equation (7.2) for the sake of clarity. In this case, the integrated dose is

\[
D(z) = 2\pi \sigma_x \sigma_y D(x_0, y_0, z),
\]

so equation (7.2) may also be expressed, in terms of \( D(z) \), as

\[
D(x, y, z) = \frac{D(z)}{2\pi \sigma_x \sigma_y} \exp \left( -\frac{(x-x_0)^2}{2\sigma_x^2} \right) \exp \left( -\frac{(y-y_0)^2}{2\sigma_y^2} \right). \tag{7.3}
\]

Let us now consider the case of a broad uniform field resulting from the superposition of an infinite number of proton pencil beams (7.3) separated a distance \( \delta x \) and \( \delta y \) between them. In this case,

\[
D(x, y, z) = \sum_{k \in \mathbb{Z}} \sum_{l \in \mathbb{Z}} D(z) \frac{1}{2\pi \sigma_x \sigma_y} \exp \left( -\frac{(x-k\delta x)^2}{2\sigma_x^2} \right) \exp \left( -\frac{(y-l\delta y)^2}{2\sigma_y^2} \right), \tag{7.4}
\]

where \( k \) and \( l \) extend over all integer numbers \( \mathbb{Z} \). Since the field is uniform by definition, equation (7.4) may be re-written as

\[
D(x, y, z) = D(0, 0, z)
\]

\[
= \frac{D(z)}{2\pi \sigma_x \sigma_y} \sum_{k \in \mathbb{Z}} \exp \left( -\frac{(k\delta x)^2}{2\sigma_x^2} \right) \sum_{l \in \mathbb{Z}} \exp \left( -\frac{(l\delta y)^2}{2\sigma_y^2} \right) \tag{7.5}
\]

\[
\equiv \frac{D(z)}{2\pi \sigma_x \sigma_y} I(x)I(y)
\]

where \( I(x) \), and \( I(y) \), are defined as

\[
I(x) = \sum_{k \in \mathbb{Z}} \exp \left( -\frac{(k\delta x)^2}{2\sigma_x^2} \right). \tag{7.6}
\]

Defining \( s_x = \sigma_x / \delta x \), equation (7.6) may be re-written as

\[
I(x) = \sum_{k \in \mathbb{Z}} \exp \left( -\frac{k^2}{2 s_x^2} \right) \approx \int_{-\infty}^{+\infty} \exp \left( -\frac{k^2}{2 s_x^2} \right) \, dk = \sqrt{2\pi} \, s_x. \tag{7.7}
\]
where in the second equality we used the Euler-McLaurin formula (Graham et al. 1990), which (i) for a Gaussian function of $s_x \geq 1$ and (ii) for the accuracy needed in radiation therapy reference dosimetry, we can safely assume to be exact. Thus, substituting $I(x)$ and $I(y)$ in equation 7.5, it follows that

$$D(0, 0, z) = \frac{D(z)}{\delta x \delta y}. \quad (7.8)$$

That is, the absorbed dose at the centre of a uniform broad field $D(0, 0, z)$ resulting from the superposition of an infinite number of proton pencil beams equally-spaced a distance $\delta x$ and $\delta y$ between them is equal to the integrated dose of a single pencil beam $D(z)$, divided by the spacing $\delta x$ and $\delta y$ between adjacent pencil beams. For divergent beams, $\delta x$ and $\delta y$ are also a function of $z$.

Note that equation (7.8) is a simple consequence of the reciprocity theorem (Attix 1986). Thus, it has been shown that, when $\delta x \leq \sigma_x$ and $\delta y \leq \sigma_y$, a broad field generated by the superposition of equally-spaced pencil beams is sufficiently uniform so that the reciprocity theorem applies.

7.3 Materials and methods

7.3.1 $D_w A$ based formalism

Making a parallelism with IAEA TRS-398 formalism based on standards of absorbed dose to water (see section 2.2.4), we propose a formalism based on standards of dose-area product, where the absorbed dose to water integrated over an area $A$ in a beam quality $Q$, $(D_w A)_Q$, in the absence of the ionization chamber, is given by

$$(D_w A)_Q = M_Q N_{DA,w,Q_0} \tilde{k}_{Q,Q_0} \quad (7.9)$$

where $M_Q$ is the reading of the ionization chamber corrected for all the quantities of influence (except for the beam quality); $N_{DA,w,Q_0}$ is the calibration coefficient of the ionization chamber in terms of dose-area product in the reference beam quality $Q_0$; and $\tilde{k}_{Q,Q_0}$ is the beam quality correction factor in terms of dose-area product.

The calibration coefficient in terms of dose-area product in the reference beam quality $Q_0$ is given by

$$N_{DA,w,Q_0} = \frac{(D_w A)_{Q_0}}{M_{Q_0}} \quad (7.10)$$

where $(D_w A)_{Q_0}$ is the absorbed dose to water at the reference depth integrated over a surface $A$ equal to the sensitive surface of the ionization chamber in the reference beam quality $Q_0$, and $M_{Q_0}$ is the reading of the ionization chamber corrected for all quantities of influence.
The beam quality correction factor in terms of dose-area product, \( \tilde{k}_{Q,Q_0} \), corrects for the different response of the ionization chamber in the user beam quality \( Q \) and the calibration beam quality \( Q_0 \). It is defined as the ratio of the ionization chamber calibration coefficients, in terms of dose-area product, at the beam qualities \( Q \) and \( Q_0 \) and it can be calculated using Monte Carlo methods as

\[
\tilde{k}_{Q,Q_0} = \frac{\tilde{f}_Q W_{\text{air},Q}}{\tilde{f}_{Q_0} W_{\text{air},Q_0}} = \frac{(D_{w,A}/\bar{D}_{\text{air}})_Q W_{\text{air},Q}}{(D_{w,A}/\bar{D}_{\text{air}})_{Q_0} W_{\text{air},Q_0}}
\]

(7.11)

where \( \tilde{f} \) is now an ionization chamber-specific and beam quality-dependent factor that establishes the proportionality between the absorbed dose to water at the reference measurement depth, in the absence of the detector, integrated over the sensitive surface the ionization chamber \((D_{w,A})\) and the average absorbed dose to air in the ionization chamber sensitive volume \((\bar{D}_{\text{air}})\).

### 7.3.2 Large-diameter ionization chamber

In this work we used a PTW 34070 Bragg Peak chamber, a large-diameter plane-parallel ionization chamber. According to manufacturer specifications, the radius of the collecting electrode is 40.8 mm, the guard ring width is 1.1 mm and the gap between the collector and the guard ring is 0.2 mm. Based on this information, we assumed the radius of the sensitive volume to be \( r = 40.9 \) mm, with an uncertainty of \( \delta r = 0.1 \) mm. The nominal thickness of the entrance window is 3.47 mm, which corresponds to a photon water-equivalent thickness of 4 mm.

### 7.3.3 Calibration in terms of \( D_{w,A} \) in a \(^{60}\text{Co} \) beam

The Bragg Peak chamber was calibrated in terms of dose-area product in the \(^{60}\text{Co} \) beam at the Swiss Federal Institute of Metrology METAS. To the extent possible, we followed the IAEA TRS-398 reference conditions for \(^{60}\text{Co} \) beams (see table 2.2). That is, we set the reference point of the chamber at a depth of 5 g cm\(^{-2}\) in water and the source-to-chamber distance to 100 cm. The reference point of the Bragg Peak chamber was taken to be the centre of the inner surface of the entrance window, i.e. 3.47 mm below the centre of the outer surface of the entrance window. The only exception with respect to the IAEA TRS-398 reference conditions was the field size, which was set to \( 22 \times 22 \) cm\(^2\), in order to guarantee a sufficiently uniform \( D_w \) across the entire chamber surface.

To be able to trace the calibration in terms of dose-area product to the METAS primary standard (water calorimeter), we performed the following steps:
1. With a secondary standard (NE 2571 Farmer chamber), we determined the ratio between \( D_w \) at the centre of the \( 22 \times 22 \text{ cm}^2 \) field and \( D_w \) at the centre of the \( 10 \times 10 \text{ cm}^2 \) reference field. We assumed the variation in the photon beam quality between calibration (\( 22 \times 22 \text{ cm}^2 \)) and reference (\( 10 \times 10 \text{ cm}^2 \)) conditions to be negligible, but we accounted for this effect in the uncertainty budget (see table 7.1).

2. With an IBA PFD-3G diode, we measured a two-dimensional \( D_w \)-map of the entire \( 22 \times 22 \text{ cm}^2 \) field, relative to the field centre. With this field map, we determined the ratio between \( D_w \) at any point in the \( 22 \times 22 \text{ cm}^2 \) field and \( D_w \) at the centre of the \( 22 \times 22 \text{ cm}^2 \) field.

With these two measurements, we obtained a two-dimensional map of the absolute \( D_w \) (because traceable to the primary standard) in the entire \( 22 \times 22 \text{ cm}^2 \) field. To determine the calibration coefficient of the Bragg Peak chamber in terms of dose-area product (7.10), we integrated \( D_w \) over the sensitive surface of the Bragg Peak chamber \((A = \pi r^2, \text{ where } r \text{ is the radius of the sensitive volume of the chamber})\). Note that \( r \) enters directly in \( N_{DA,w,Q_0} \). Thus, the uncertainty of this value has a direct impact on the uncertainty of \( N_{DA,w,Q_0} \).

Finally, it should be mentioned that our calibration is terms of dose-area product assumes a uniform response of the Bragg Peak chamber across the entire sensitive surface. In reality, however, the pressure of water against the thin entrance window causes a slight decrease in the distance between the front and collecting electrodes, which is more pronounced in the central part of the chamber. This effect was assumed to be negligible, but it was accounted for in the uncertainty budget based on information provided by the manufacturer (see table 7.1).

7.3.4 Monte Carlo calculation of \( \tilde{k}_Q \) factors

The beam quality correction factor of the PTW Bragg Peak chamber in proton beams was calculated similarly as in chapter 6. In what follows, only the differences with respect to chapter 6 are described.

First of all, we calculated the \( \tilde{k}_Q \) factors based on equation (7.11), i.e. in terms of dose-area product. As reference conditions for the reference beam quality \(^{60}\text{Co} \) we defined a \( 40 \times 40 \times 15 \text{ cm}^3 \) water phantom and we set the reference depth to \( 5 \text{ g cm}^{-2} \), the source-to-chamber distance to \( 100 \text{ cm} \) and the field size at the reference depth to \( 22 \times 22 \text{ cm}^2 \). For proton beams we defined a \( 40 \times 40 \times 5 \text{ cm}^3 \) water phantom, we set the reference depth to \( 2 \text{ g cm}^{-2} \) and the field size to \( 22 \times 22 \text{ cm}^2 \).

The \( D_wA \) at the reference depth was calculated as the average absorbed dose to water scored in a disc of 40.8 mm of radius and 250 \( \mu \text{m} \) of thickness, centred on the central axis of the beam at the reference depth. \( D_{\text{air}} \)
was calculated as the average absorbed dose to air in the Bragg Peak chamber sensitive volume—here assumed to have a sensitive radius according to manufacturer specifications ($r = 40.8$ mm). For both $^{60}$Co and proton beams the reference point of the chamber was positioned on the central axis of the beam at the reference depth.

As $^{60}$Co beam source we simulated a monoenergetic 1.25 MeV photon point source located 100 cm away from $z_{\text{ref}}$ (i.e. 95 cm away from the water phantom surface), shaping a $22 \times 22$ cm$^2$ field at the reference depth. As proton source we generated a $22 \times 22$ cm$^2$ phase-space file at a depth of 15 mm in water with GAMOS for five different proton energies: 70, 100, 150, 200 and 250 MeV.

Finally, we also calculate the $k_Q$ factor of the PTW Markus chamber as described in chapter 6, but with a monoenergetic 1.25 MeV photon source as reference beam quality.

### 7.3.5 Experimental determination of $D_w A$ of a proton pencil beam

With the large-diameter ionization chamber, we determined the $D_w A$ of different quasi-monoenergetic proton pencil beams (with energies ranging from 70 to 230 MeV, in 10 MeV energy steps) using equation (7.9). The reference point of the Bragg Peak chamber was set at a reference depth of 2 g cm$^{-2}$ in water. The $\tilde{k}_Q$ factors were interpolated from the values calculated with Monte Carlo simulation for 70, 100, 150, 200 and 250 MeV monoenergetic proton beams. Also in this case the water pressure causes a slight decrease in the distance between the front and collecting electrodes, more pronounced in the central part of the chamber—which is precisely where the proton pencil beam impinges. This effect was again assumed to be negligible, but it was accounted for in the uncertainty budget with a relative standard uncertainty of $u = 0.12\%$.

Additionally, we determined $D_w A$ for the same quasi-monoenergetic proton energies with a conventional ionization chamber using equation (7.8). That is, we determined $D_w$ at the centre of a $10 \times 10$ cm$^2$ field with a PTW Markus chamber (previously calibrated in terms of $D_w$ at METAS) as described in chapter 4. The reference point of the chamber was set at a reference depth of 2 g cm$^{-2}$ in water and the broad $10 \times 10$ cm$^2$ field was generated by the superposition of proton pencil beams equally-spaced by a distance $\delta x = \delta y = 2.5$ mm. The $k_Q$ factors were interpolated from the values calculated with Monte Carlo simulation.

### 7.4 Results and discussion

Table 7.1 shows the comparison between the uncertainty estimates of the calibration coefficient of the Markus chamber (in terms of absorbed dose to
Table 7.1: Estimated relative standard uncertainty of all the components entering in the determination of the calibration coefficients in terms of $D_w$ of a Markus chamber and in terms of $D_w A$ of a Bragg Peak chamber in the $^{60}$Co beam at METAS. The combined relative standard uncertainty of the calibration coefficients is also shown. All values are in %.

<table>
<thead>
<tr>
<th></th>
<th>$N_{D_{w}}^{\text{Markus}}$</th>
<th>$N_{D_{w}}^{\text{bpc}}$</th>
<th>$N_{D_{w}A}^{\text{Markus}}$</th>
<th>$N_{D_{w}A}^{\text{bpc}}$</th>
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</thead>
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<tr>
<td></td>
<td>$u_A$</td>
<td>$u_B$</td>
<td>$u_A$</td>
<td>$u_B$</td>
</tr>
<tr>
<td>$D_{w,10\times10}^{\text{cal}}$</td>
<td>0.36</td>
<td></td>
<td>0.36</td>
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<tr>
<td>$H_{10\times10}^{\text{cal}}$</td>
<td>0.05</td>
<td>0.11</td>
<td>0.05</td>
<td>0.11</td>
</tr>
<tr>
<td>$H_{10\times10}^{\text{Markus}}$</td>
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<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$M_{10\times10}^{\text{Markus}}$</td>
<td>0.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- $k_{PT}$</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- $k_{h}$</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- $k_{\text{elec}}$</td>
<td>0.06</td>
<td></td>
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<tr>
<td>- $k_{a}$</td>
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<td></td>
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<tr>
<td>- $k_{z}$</td>
<td>0.07</td>
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<tr>
<td>$H_{2s,10\times10}^{2s}$</td>
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<td>0.02</td>
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</tr>
<tr>
<td>$M_{2s,10\times10}^{2s}$</td>
<td>0.01</td>
<td>(correlated)</td>
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</tr>
<tr>
<td>$H_{22,22}^{22}$</td>
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<td></td>
</tr>
<tr>
<td>$M_{22,22}^{22}$</td>
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<td>(correlated)</td>
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<tr>
<td>- $k_{Q22,22,10\times10}^{Q}$</td>
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<td>$H_{22,22}^{\text{bpc}}$</td>
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<td>$M_{22,22}^{\text{bpc}}$</td>
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<td>- $k_{PT}$</td>
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<tr>
<td>- $k_{h}$</td>
<td>0.03</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- $k_{\text{elec}}$</td>
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<tr>
<td>- $k_{a}$</td>
<td>0.01</td>
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<td></td>
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<tr>
<td>- $k_{z}$</td>
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<td>- $k_{\text{water pressure}}$</td>
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<td></td>
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<td>$A_{\text{bpc}}$</td>
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</tr>
<tr>
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<td>0.39</td>
<td>0.17</td>
<td>0.52</td>
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<tr>
<td>Combined $u_C$</td>
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<td></td>
<td>0.54</td>
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</table>
Table 7.2: Monte Carlo calculated \( \tilde{k}_Q \) factors of the PTW Bragg Peak chamber in monoenergetic proton beams, at the reference depth of 2 g cm\(^{-2} \), as a function of the initial proton energy. \( I_w = 75 \text{eV}, I_g = 78 \text{eV} \) and \( W_{\text{air,Q}}/W_{\text{air,Q}_0} = 1.008 \). The values within parenthesis correspond to one standard uncertainty in the last digit.

<table>
<thead>
<tr>
<th>E (MeV)</th>
<th>( \tilde{k}_Q )</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>0.990(5)</td>
</tr>
<tr>
<td>100</td>
<td>0.997(5)</td>
</tr>
<tr>
<td>150</td>
<td>1.001(5)</td>
</tr>
<tr>
<td>200</td>
<td>1.002(5)</td>
</tr>
<tr>
<td>250</td>
<td>1.001(5)</td>
</tr>
</tbody>
</table>

water) and the calibration coefficient of the Bragg Peak chamber (in terms of dose-area product), in the \(^{60}\text{Co} \) beam at METAS. The superscripts \( \text{cal}, \text{2s} \) and \( \text{bpc} \) stand for water calorimeter, secondary standard (NE 2571) and Bragg Peak chamber, respectively. The subscripts 10 \( \times \) 10 and 22 \( \times \) 22 refer to the field size in cm\(^2 \). \( H \) is the correction factor for field homogeneity, \( M \) is the reading of the ionization chamber and \( A_{\text{bpc}} \) is the integration surface of the Bragg Peak chamber. For instance, \( H_{\text{cal}}^{10 \times 10} \) is the correction factor that accounts for the difference between the average \( D_w \) integrated over the sensitive surface of the water calorimeter and the ‘point’ \( D_w \) at the centre of the reference 10 \( \times \) 10 cm\(^2 \) field.

Table 7.1 shows that the uncertainty estimate of the calibration coefficient in terms of dose-area product \( (u_C = 0.5\%) \) is slightly larger than the uncertainty of the calibration coefficient in terms of absorbed dose to water \( (u_C = 0.4\%) \). This is mainly due to the uncertainty of the sensitive area of the Bragg Peak chamber, where a small uncertainty in the integration radius \( (\delta r = 0.1 \text{mm}) \) leads to a relatively large uncertainty in the integration surface \( (u_B = 0.3\% \), see table 7.1). Table 7.2 shows the Monte Carlo calculated \( \tilde{k}_Q \) factors of the PTW Bragg Peak chamber in monoenergetic proton beams, at the reference depth of 2 g cm\(^{-2} \), as a function of the initial proton energy. The variation of the \( \tilde{k}_Q \) factors with the initial energy of the proton beam follows the same trend than the \( k_Q \) factors of plane-parallel chambers in table 6.5.

Finally, figure 7.1 shows the comparison between the determination of \( D_w A \) (per MU) of a single proton pencil beam with the Bragg Peak chamber using equation (7.9) and with the Markus chamber using equation (7.8). Note that figure 7.1(a) shows an alternative approach to the calibration of proton beam monitor chambers to the one described in chapter 4—i.e. the calibration curve shown in figure 7.1(a) (in terms of \( D_w A/\text{MU} \)) is inversely proportional to the one shown in figure 4.1 (in terms of \( \text{MU}/p \)). Figure 7.1 shows that the two approaches to the determination of \( D_w A \) of a proton pencil beam agree with each other within 1.5\% or better. Note that,
Figure 7.1: (a) $D_{wA}$ at the reference depth of a proton pencil beam per MU, as a function of proton energy, determined with the Bragg Peak chamber (○) and the Markus chamber (⋄). (b) Ratio between the Bragg Peak chamber and the Markus chamber $D_{wA}$ determination. The uncertainty bars correspond to one standard uncertainty.
whereas the two beam monitor chamber calibration curves in figure 7.1(a) agree with each other within one standard uncertainty, the ratio between the two curves in figure 7.1(b) does not. This is due to the fact that some components entering in the determination of $D_wA$ (e.g. the absorbed dose to water under reference conditions determined with water calorimetry, $D_{w,10\times10}^{\text{cal}}$), cancel out in the ratio between the two calibration curves, leading to a smaller combined standard uncertainty. Note also that uncertainties are typically larger for low-energy proton beams. This is due to the fact that the uncertainty in the ionization chamber reading caused by the uncertainty in setting up the ionization chambers at the reference depth (denoted by $k_z$ in table 7.1 for $^{60}$Co) is larger for low-energy proton beams, because of the steeper dose gradient at the reference depth of 2 g cm$^{-2}$. Figure 7.1(b) shows that the average difference between the two approaches is smaller than 0.7% with an average standard uncertainty of 0.8%. These differences seem to have an energy-independent component, resulting from some of the underlaying assumptions in the calibration in terms of $D_wA$ in the $^{60}$Co beam discussed above, as well as an energy-dependent component, resulting mainly from the assumptions and approximations used in the Monte Carlo calculation of the beam quality correction factors of the two ionization chambers.

7.5 Conclusions

This chapter describes a novel approach to the reference dosimetry of proton pencil beams based on the concept of dose-area product. This approach, based on the determination of the dose-area product of a single proton pencil beam, was shown to be feasible, because it yielded equivalent results to the standard approach based on the determination of the absorbed dose to water in the centre of a broad field. Nevertheless, further research needs to be done in order to reduce the uncertainty associated to this new method and to bring the two approaches in better agreement.

It is believed that the main drawback of this novel approach is that the sensitive surface of the large-diameter ionization chamber must be known with a high-level of accuracy, so as not to ruin the uncertainty of the calibration coefficient in terms of dose-area product. Because of this requirement, the uncertainty of the calibration coefficient in terms of dose-area product will always be larger than the uncertainty of the calibration coefficient in terms of absorbed dose to water.

Nonetheless, there might be cases where a slightly larger uncertainty in the calibration coefficient could pay off. An example could be the reference dosimetry of small photon beams, where other factors—such as the size of the detector—might result in a larger source of uncertainty in the determination of the absorbed dose to water at a point.
The main goal of this thesis was to improve the accuracy and reduce the uncertainty in the radiation dosimetry of clinical proton beams. In order to do so, this work used Monte Carlo simulations to calculate water/medium stopping-power ratios—necessary for relative and reference dosimetry—and beam quality correction factors—the cornerstone of reference dosimetry. Monte Carlo calculations were validated with experimental measurements comparing reference dosimetry with Faraday cup dosimetry, and comparing the response of different ionization chambers in $^{60}$Co and proton beams to determine an experimental ratio of beam quality correction factors. Finally, a novel approach to the reference dosimetry of proton pencil beams was described.

Concerning relative dosimetry, it was found that air and radiochromic film active layer are the most suitable detection materials for depth-dose measurements in water; whereas the use of silicon and gadolinium oxysulfide should be discouraged. As for lateral dose profiles and field-specific dose distribution measurements in water, it was found that air, radiochromic film active layer, lithium fluoride and silicon are all appropriate detection materials. For lateral dose profiles and field-specific dose distribution measurements in air, it is believed that gadolinium oxysulfide could also be used. Overall, it was found that the relative dosimetry of low-energy proton beams is more demanding than the one of high-energy proton beams.

Concerning reference dosimetry, it was found that protons are, to a very good approximation, the only particles that need to be included in the calculation of water/air stopping-power ratios—including electrons increases systematically $s_{w,air}$ values by 0.1%, whereas including track-ends and particles heavier than protons has no effect on $s_{w,air}$ ratios.

The Monte Carlo beam quality correction factors calculated in this work were found to agree within 2.3% with the tabulated values in IAEA TRS-398 (and within 1% with experimental values obtained with water calorimetry). Despite this agreement, the results of this work seem to indicate that per-
turbation correction factors in proton beams could be significantly different from unity, at least for some of the ionization chambers studied here.

The comparison between reference dosimetry based on IAEA TRS-398 and Faraday cup dosimetry was found to agree within approximately 3%—that is within two standard uncertainties. Nevertheless, when using the Monte Carlo $k_Q$ factors calculated in this work, the two independent dosimetry techniques were found to agree within approximately 1.5%.

This comparison also detected a systematic error in the determination of the absorbed dose to water, especially relevant for low-energy proton beams, when using cylindrical chambers together with IAEA TRS-398 reference conditions for monoenergetic proton beams. This error arises from the IAEA TRS-398 recommendation of positioning the reference point of cylindrical chambers at the reference depth. There are two different strategies to correct this systematic error: (i) to position the effective point of measurement of cylindrical chambers—not the reference point of measurement—at the reference depth (as discussed in chapter 4) or (ii) to include the correction for dose gradient effects in the beam quality correction factor (as in chapters 5 and 6).

The adoption of new mean excitation energy values for water and graphite has an effect on both the water/air stopping-power ratios and the beam quality correction factors for proton beams. A difference of 3 eV in $I_w$ results in a difference of approximately 0.6% in the $s_{w,\text{air}}$ values. In the same vein, a difference of 3 eV in both $I_w$ and $I_g$ may results in differences up to 1.6% in the $k_Q$ factor of certain ionization chambers. The uncertainty of $I$-values is nowadays the largest source of uncertainty of water/air stopping-power ratios and beam quality correction factors for proton beams.

It is believed that the results of this work could contribute to improve the accuracy and reduce the uncertainty in the reference dosimetry of proton pencil beams—if taken into consideration in future dosimetry guidelines for clinical proton beams. It is of utmost importance that the radiation dosimetry of clinical proton beams is performed uniformly and consistently throughout the world, so that clinical experience can be transferred between different proton therapy centres. Thus, this work encourages the use of internationally agreed guidelines to determine the absorbed dose to water in clinical proton beams. As of today, these guidelines are the IAEA TRS-398 Code of Practice for proton beams. In this case, the results of this work seem to indicate that the use of plane-parallel chambers is preferable (to cylindrical chambers) for the reference dosimetry of non-modulated proton beams.

Finally, this work described a novel approach to the reference dosimetry of proton pencil beams based on the dose-area product, which was proved to be feasible by showing it yielded equivalent outcome to the standard approach based on the determination of the absorbed dose to water at a point. Its only disadvantage is a larger uncertainty in the ionization chamber
calibration factor. This disadvantage, however, could pay off in the radiation dosimetry of other types of external radiotherapy beams.

Additional research needs to be done to further improve the accuracy and reduce the uncertainty in the radiation dosimetry of clinical proton beams. First, there is a need of a more accurate and precise determination of the mean excitation energy values of the different materials relevant to the reference dosimetry of proton beams. Second, there is also the need of Monte Carlo simulation tools which include all proton interactions with matter, together with a detailed simulation of charged particle transport. That could be achieved, for instance, by introducing proton nuclear interactions in PENH.
References


D. T. Burns (2003). ‘Calculation of $k_{\text{wall}}$ for $^{60}\text{Co}$ air-kerma standards using *penelope’*. CCRI(I)/03-40.


