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Dosimetry of Carbon-Ion Reference and Small Photon Fields for Magnetic Resonance-Guided Radiation Therapy

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Abstract

Magnetic resonance-guided radiation therapy (MRgRT) enables online adaptive treatment planning and beam delivery based on the visualization of actual location of tumor and normal tissues. This allows for the better tumor coverage and normal tissue sparing. However, magnetic fields affect the dose distribution and the detector response, demanding correction for accurate dose measurements. This thesis investigates the response alteration of six Farmer-type ionization chambers in a carbon ion reference field in presence of magnetic fields of 0.1 to 1 T. A complex dependency on magnetic field strength and chamber volume was obtained with maximum corrections of 0.6 %. Measurements and Monte Carlo simulations revealed a good agreement. Additionally, small field characteristics of photon fields at the 6 MV/0.35 T ViewRay MR-Linac were investigated. Output factors for small fields were measured for two different detectors (PTW PinPoint 3D and microDiamond) for isocentric square and rectangular fields as well as for off-axis fields. Field output factors obtained from Monte Carlo calculations were used to derive output correction factors, which may be used when performing clinical dosimetry of small fields. The derived correction factors reduce the uncertainties of dose measurements in carbon ion reference and small photon fields in presence of magnetic fields.

Zusammenfassung

Die Magnetresonanz-geführte Strahlentherapie (MRgRT) ermöglicht eine online adaptierte Behandlungsplanung und Bestrahlung auf Basis der Visualisierung der tatsächlichen Lage von Tumor und des Normalgewebe. Dies ermöglicht eine bessere Abdeckung des Tumors und die Schonung des Normalgewebes. Allerdings beeinflussen Magnetfelder die Dosisverteilung und das Ansprechvermögen des Detektors, was für genaue Dosismessungen eine Korrektur erfordert. In dieser Arbeit wird die Veränderung des Ansprechverhaltens von sechs Farmer-Ionisationskammern in einem Kohlenstoffionen-Referenzfeld in Gegenwart von Magnetfeldern der Stärke 0.1 bis 1 T untersucht. Es wurde eine komplexe Abhängigkeit von Magnetfeldstärke und Kammervolumen mit maximalen Korrekturen von 0.6 % festgestellt. Messungen und Monte-Carlo-Simulationen ergaben eine gute Übereinstimmung. Zusätzlich wurden die Eigenschaften kleiner Photonenfelder am 6 MV/0.35 T ViewRay MR-Linac untersucht. Die Outputfaktoren für kleine Felder wurden für zwei verschiedene Detektoren (PTW PinPoint 3D und microDiamond) sowohl für isozentrische quadratische und rechteckige Felder als auch für exzentrische Felder gemessen. Die aus Monte-Carlo-Berechnungen gewonnenen Feld-Outputfaktoren wurden zur Ableitung von Output-Korrekturfaktoren verwendet, die in der klinischen Dosimetrie von kleinen Feldern eingesetzt werden können. Die abgeleiteten Korrekturfaktoren verringern die Unsicherheiten von Dosismessungen in Kohlenstoffionen-Referenz- und kleinen Photonenfeldern in Gegenwart von magnetischen Feldern.

*“ Though free to think and act, we are held together,
like the stars in the firmament, with ties inseparable.
These ties cannot be seen, but we can feel them.”*

Nikola Tesla

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Glossary

CAX	<i>central axis</i>
CPE	<i>charged particle equilibrium</i>
CSDA	<i>continuous slowing down approximation</i>
CT	<i>computed tomography</i>
EGS	<i>Electron Gamma Shower</i>
EMPIR	<i>European Metrology Programme for Innovation and Research</i>
ERE	<i>electron return effect</i>
FFF	<i>fattening filter-free</i>
FWHM	<i>full width at half maximum</i>
IAEA	<i>International Atomic Energy Agency</i>
IgRT	<i>image-guided radiation therapy</i>
IMRT	<i>intensity-modulated radiation therapy</i>
LCPE	<i>lateral charged particle equilibrium</i>
MC	<i>Monte Carlo</i>
MLC	<i>multi-leaf collimator</i>
MRI	<i>magnetic resonance imaging</i>
MRgRT	<i>magnetic resonance-guided radiation therapy</i>
MU	<i>monitor unit</i>
MV	<i>mega-volt</i>
MeV/u	<i>megaelectron-volt per unified atomic mass unit</i>
NPL	<i>National Physical Laboratory</i>
PDD	<i>percentage depth dose</i>
PMMA	<i>polymethyl methacrylate</i>
PSDL	<i>Primary Standard Dosimetry Laboratories</i>
RMSE	<i>root mean square error</i>
RT	<i>Radiation therapy</i>
SAD	<i>source-to-axis distance</i>
SOBP	<i>spread-out Bragg peak</i>
SSD	<i>source surface distance</i>
TOPAS	<i>Tool for Particle Simulation</i>
TRS	<i>Technical Report Series</i>

1 Introduction

1.1 Radiation therapy

Cancer is a disease characterized by the uncontrolled proliferation of cancerous cells. These cells may form lumps of tissue (tumors) and have the ability to infiltrate nearby tissues or generate distant tumors growth through a process known as metastasis [1]. Radiation therapy (RT) applies ionizing radiation to damage the genetic material of cancer cells, inhibiting their division and proliferation, ultimately leading to their destruction [2]. Approximately 50 % of all cancer patients worldwide receive RT as part of their treatment [3]–[5]. An important quantity in RT is the radiation dose, defined as the amount of energy deposited by ionizing radiation per unit mass in a medium. The aim of RT is the escalation of the radiation dose to the cancer cells while minimizing the impact on the cells of surrounding healthy tissues[6]–[8]. To reach this aim, the design of radiation treatments has to be tailored to the unique characteristics of each patient. Yet, the highly precise dose delivery in RT presents challenges due to uncertainties in patient setup, imaging, treatment planning and delivery [9].

A megavoltage X-ray photon beam delivered by a linear accelerator (Linac) is the most commonly used radiation type for cancer treatment worldwide [10]. These photon beams are generated when high-energy electrons, typically within a range of 6 to 18 MeV, are accelerated by the Linac and hit a high atomic number target (e.g., tungsten). This interaction leads to the emission of characteristic X-rays and Bremsstrahlung photons [10]. The generated photon beam exhibits a forward-peaked distribution. To achieve beam uniformity, a flattening-filter (FF) is traditionally used. In modern Linacs, however, the flattening filter is often omitted leading to a flattening filter-free (FFF) photon beam. This approach increases dose rate and reduces the treatment time. This is particularly advantageous for small fields and intensity-modulated radiation therapy (IMRT) where the flatness of the beam is not required [11]–[13]. While medical Linacs are commonly used for photon irradiation, they can be also used as an electron source by replacing the target by a scatter foil [10]. A typical dose distribution of a megavoltage photon beam in tissue initially experiences a rapid increase (build-up region), followed by an exponential decrease with depth (see Figure 2.1). Compared to photons, electron beams experience a higher dose at the surface that decreases rapidly towards the maximum range of the electrons. Therefore electron beam provides a clinical advantage over conventional photon beam in the treatment of superficial tumors [14].

For photons, the integration of multi-leaf collimators (MLCs) within Linacs enabled significant improvements in precise shaping of the dose distribution. MLCs consist of movable leaves (normally made of tungsten) that selectively block part of the radiation beam, allowing for the desired treatment shape. This technique has been extensively used also for small photon fields, down to the subcentimeter scale [15].

Many modern RT techniques, such as IMRT, volumetric modulated arc therapy (VMAT), and stereotactic radiosurgery (SRS), among others, deliver the radiation beam by the use of Linacs

[16], [17]. These techniques can employ either single small fields to irradiate small target volumes, or multiple small fields to compose larger fields. The gantry of Linacs, which rotates around the patient, allows beam delivery from various angles to shape larger target volumes while sparing healthy tissue.

In addition to electrons and photons, RT is also carried out with protons and light ions. The most common ion types used worldwide are protons and carbon ions. Recently, helium ions were used for the first time at the Heidelberg Ion-Beam Therapy Center (HIT) in Germany to treat a patient [18]. To reach energies for therapeutic purposes, protons can be accelerated using cyclotron or synchrotron accelerators. However, for accelerating carbon ions synchrotrons are needed. Compared to photon beams, protons and carbon ions exhibit an inverse depth dose distribution, i.e. the dose increases with depth until the maximum range of the particles is reached. This makes them an advantageous tool for treating deep-seated tumors [19]. Dose distributions of proton and carbon ions are characterized by a sharp maximum known as the Bragg peak (see Figure 2.1) [20], [21]. The peak is typically very narrow, spanning a few millimeters at the 80 % dose level and is several times higher than the plateau region [21]. By tailoring the Bragg peak within the tumor region, surrounding healthy tissue along the beam path prior to and beyond the peak can be effectively spared. The position of the Bragg peak can be adjusted in depth by changing the energy of the particles. However, due to the narrowness of the peak, it becomes necessary to broaden it, creating what is known as a spread-out Bragg peak (SOBP) for treatment. The SOBP is generated by superimposing Bragg-peaks of different energies [22]. In comparison to protons, carbon ions offer several advantages. Due to the higher mass, carbon ions scatter less than protons resulting in narrower pencil beam. Additionally, carbon ions offer a significantly higher biological effectiveness as compared to protons, especially in the presence of hypoxic regions in the tumor [23]. This characteristic makes carbon ions suitable for achieving both effective physical and biological dose localization [21].

However, the effectiveness of RT delivery techniques depends on the accuracy of dose delivery, which may be compromised by setup error or inter- and intra-fractional motion of the patient. Medical imaging technology is utilized to localize tumor and surrounding organs at risk and use this information to prevent overdosage to healthy tissue and underdosage to the tumor volume. Normally, the dose distribution is calculated based on computed tomography (CT) images during the treatment planning phase. Safety margins are added around the tumor volume to account for potential uncertainties in patient positioning, tumor motion, and any other possible uncertainty source, and to ensure the dose coverage of the tumor [24]. Recently, it became possible to image the patient anatomy during or directly before the treatment. This technique, known as image-guided radiation therapy (IGRT), enhances the precision of dose delivery by minimizing uncertainties related to patient positioning and target localization. As a result, margins can be potentially reduced [25] thereby sparing the surrounding healthy tissue.

1.2 Magnetic resonance-guided radiation therapy

Among all imaging techniques used for IGRT, magnetic resonance imaging (MRI) stands out in terms of high soft-tissue contrast with no additional imaging dose delivered to the patient.

Magnetic resonance-guided radiation therapy (MRgRT) enables adaptive treatment planning based on the visualization of soft tissue. In conventional radiation therapy, patients are positioned according to the treatment plan initially calculated using CT images. In contrast, MRgRT allows for the adaptation of the treatment plan to match the actual patient anatomy on the day of treatment [26].

MRgRT enables patient treatments based on MR images acquired either at a separate device before treatment (offline system) or at the treatment device (MR-Linac) directly before or even during the treatment (online system). In offline MRgRT, patient can be transported from the MRI scanner to the treatment device in treatment position ('shuttle system') [27], [28] or the MRI itself can be mounted on rail system ('MRI-on-rails') [29], [30].

Online MRgRT involves the use of special hybrid devices that combine a radiotherapy unit with an integrated MRI scanner. These devices are implemented in clinical routine with MR-Linacs for photon therapy. Currently, there are two commercially available MR-Linacs: the 0.35 T and 6 MV FFF MRIdian machine (ViewRay Inc., Oakwood, USA) [31], [32], and the 1.5 T and 7 MV FFF Elekta Unity machine (Elekta Instrument AB, Stockholm, Sweden) [33], [34]. Online MRgRT also allows for real-time adaptation of the treatment plan directly on the treatment table. This includes tracking of the moving targets or automated beam gating [35]–[38]. Tracking involves adjusting the beam to follow the tumor motion, while gating involves activating the beam only when the tumor reaches a specific position.

The construction of such a hybrid machine, similar to MR-Linac, for ion beam RT is currently investigated [39], [40]. Due to the steep gradients in the depth dose profiles, dose distribution generated with ions are less robust to setup and motion than dose distributions generated with photons (Figure 2.1). Therefore, ion beam RT is expected to benefit even more from MR-guidance.

However, the magnetic field in hybrid machines comes along with additional dosimetric challenges. Dose measurements in online MRgRT have to be performed in the presence of static magnetic field, which affects the dose distribution as well as the detector response. To ensure high accuracy of the MRgRT devices, dosimetry in magnetic field for both, photons and ions, has to be further investigated.

1.3 Challenges of dosimetry in magnetic fields

Dosimetry in the presence of magnetic fields is challenging due to the deflection of charged particles by the Lorentz force. In photon therapy, interactions between photons and matter lead to the production of secondary electrons, which are affected by this force. These secondary electrons have an impact on the dose distribution. In ion-beam therapy, both primary ions and secondary charged particles (e.g., electrons), are affected by the Lorentz force. Nonetheless, the

predictable curved path of ion beams in a magnetic field can be accounted for during the treatment planning process [40].

The deflection of secondary electrons in magnetic fields can change the response of ionization chambers that are typically used for reference dosimetry. Due to variations in the trajectories of secondary electrons within magnetic fields compared to non-magnetic field conditions for which the chamber is calibrated, the ionization chamber fails to report the actual dose. To correct for the impact of magnetic fields on the detector response in the reference field and for the change in the local dose distribution, magnetic field correction factors $k_{\vec{B},Q}$ are proposed. To date, official international protocols for reference dosimetry, such as TRS-398 [41], do not include magnetic field condition. However, in recent years, the scientific literature has reported on $k_{\vec{B},Q}$ values for ionization chambers in MR-Linacs [42]–[48].

Furthermore, dosimetry of small fields, still pose a challenge due to perturbations of the charged particle equilibrium. In the context of MRgRT, the magnetic field produces asymmetric lateral dose distributions around the central axis of the field. This effect is particularly pronounced for small fields and has to be further investigated by profile measurements. Small photon fields additionally need output correction factors in the presence of a magnetic field $k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$. However, the official dosimetry protocol for small photon fields TRS-483 [49] does not provide any corrections in presence of magnetic fields. This highlights the need to investigate these corrections for commercially available MR-Linacs.

As developments in ion beam MRgRT are lagging behind photon MRgRT, reference dosimetry for ion beams in magnetic fields has not reached the same level as for photon beams and the available literature on this topic is still limited. Although, recent studies reported $k_{\vec{B},Q}$ values for proton beams in a range of 0 T to 1 T magnetic field [50], [51], no studies have investigated $k_{\vec{B},Q}$ for carbon-ion beams. At the time of writing the thesis, the first publication in this field demonstrated experimentally determined $k_{\vec{B},Q}$ values for carbon-ion beam in a range of 0 T to 1 T magnetic field [52]. Therefore, investigation towards dosimetry in reference carbon-ion beams in magnetic fields is of high importance.

1.4 Aim and outline of the thesis

Standardized methodologies for dose measurements in the presence of magnetic fields are scarce. Therefore, the full clinical implementation of MRgRT faces challenges specifically in dosimetry. Existing dosimetry protocols have not yet addressed dose measurements in magnetic fields. Hence, there is a strong need to calculate correction factors and develop methodologies for dosimetry in MRgRT. This thesis is divided into two parts as explained in the following.

Although ion beam MRgRT technology is lagging behind photon beam MRgRT, the ability to perform accurate dose measurements and to investigate the suitability of existing detectors is a prerequisite for the development of ion beam MRgRT. However, no dosimetry protocol traceable to primary standards is available for ion-beam MRgRT. Therefore, the first part of this project examines the response of ionization chambers in carbon-ion beams under reference conditions in presence of magnetic fields utilizing the current TRS-398 recommendations. This project aims to investigate the ionization chambers response in carbon-ion beams as a function of the magnetic flux density and the chambers volume. The investigation results in magnetic field correction factors $k_{\vec{B},Q}$ for six chambers with varying inner radii through a combined approach of experimental measurements and Monte Carlo simulations.

The second part of the project focused on MR-guided photon therapy, going one step beyond to investigate dosimetry of small fields in presence of magnetic fields. In conventional large fields, the ratio of the absorbed dose to water in small field to that in a reference field at a specific depth (field output factor) is approximated by the ratio of detector readings (output factor). However, in the case of small fields due to non-equilibrium conditions, this approximation is not valid. Therefore, the measured detector reading ratios need to be corrected using the output correction factors $k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$. For the absence of magnetic fields, these output correction factors are outlined in the well-established TRS-483 dosimetry protocol for small fields. For use in presence of magnetic fields, TRS-483 needs to be extended. Within the international EMPIR (European Metrology Programme for Innovation and Research) funded project “Traceable Dosimetry for Small fields in MR-guided RadioTherapy (MRgRT-DOS)” [53], a methodology was developed to determine output correction factors $k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$. Within this thesis, this methodology was applied for the clinical MR-Linac (ViewRay MRIdian machine) operating in the presence of a 0.35 T magnetic field. The aim was to determine output correction factors in the presence of a magnetic field for two frequently used detector types through a combination of experimental measurements and Monte Carlo simulations.

This thesis is structured in five chapters. Following the introductory section, Chapter 2 presents materials and methods employed in the research. Here, the physical foundations of radiation interactions in matter are introduced, setting the groundwork for the absorbed dose determination. This chapter also introduces the basic quantities of radiation dosimetry. Furthermore, the formalism for clinical reference and relative dosimetry of small fields is

presented, with a notable extension to the magnetic field conditions as developed in the MRgRT-DOS project. The subsequent sections are divided into two projects: '*Carbon-ion reference dosimetry in magnetic fields*' and '*Small photon field dosimetry in magnetic fields*'. The experiments conducted for both projects are explained, followed by the corresponding Monte Carlo simulations. Chapter 3 is dedicated to the results achieved in both projects, providing a comprehensive overview of the outcomes and findings. In Chapter 4, a detailed discussion of the results from both projects is provided, enabling a deeper understanding of the implications and significance of the obtained data. Finally, Chapter 5 presents the main conclusions from this thesis.

2 Materials and methods

2.1 Interactions of radiation with matter

Understanding the basic interactions between radiation and matter that result in energy deposition is essential for determining absorbed dose. The biological effects in radiation therapy correlate with absorbed dose, emphasizing the importance of understanding the underlying physical processes.

Radiation can be classified into two primary categories: non-ionizing and ionizing, based on its ability to ionize matter. Ionization refers to the process of removing electrons from atoms, resulting in the formation of charged particles. Directly ionizing radiation, which includes charged particles, such as electrons, protons, or carbon-ions, deposits energy in a medium by directly interacting with the orbital electrons of the atoms within the medium. On the other hand, indirectly ionizing radiation, such as photons or neutrons, deposits energy in a medium through a two-step process. In the first step, the radiation interacts with the medium and releases secondary charged particles, such as electrons or positrons. In the second step, these released secondary electrons deposit their energy in the medium through direct interactions with atomic electrons [14].

Radiation may undergo various interactions with matter. The probability that these interactions occur is defined as cross-section, denoted by σ . However, the cross section depends on various factors, including the type and energy of the radiation, and the atomic number Z of the traversed material [14]

2.1.1 Interactions of photons

Photons indirectly deposit energy in matter mainly via secondary electrons. Released secondary electrons undergo Coulomb interactions with atomic orbital electrons in matter resulting in local dose deposition. Within the energy range of radiation therapy, photons transfer their energy to electrons through three main types of interactions: the photoelectric effect, Compton effect, and pair production. As a result of these interactions, photons can either be absorbed or scattered. [14]

In the photoelectric effect, the photon interacts with tightly bound electrons from the inner shells of an atom. Here, the photon transfers its entire energy to the electron, leading to the complete absorption of the photon. The released electron carries a kinetic energy equal to the difference between the energy of the incident photon and the binding electron energy. The photoelectric effect is the most dominant interaction for low-energy photons.

The Compton effect describes the interaction of a photon with a free or loosely bound electron, where a portion of the photon's energy is transferred to the recoiling electron. As a result of this

interaction, the electron is released from the atom, and the photon scatters in a different direction with reduced energy. The Compton effect is dominant for photon energies typically ranging from 0.1 to 10 MeV.

Pair production is another interaction process where a photon is absorbed, resulting in the creation of an electron-positron pair. This process can only occur in the presence of a Coulomb force field, usually near to the atomic nucleus. Pair production becomes energetically possible when photon energy $h\nu$ exceeds $2m_e c^2 = 1.022 \text{ MeV}$, where $m_e c^2$ is the rest energy of electron and positron [54].

These three interactions lead to the attenuation of the photon beam. For an attenuation after a thickness x , the unattenuated photon beam intensity $I(0)$ decreases exponentially to $I(x)$ according to the equation:

$$I(x) = I(0) e^{-\mu(h\nu, Z)x}, \quad (2.1)$$

where μ represents the linear attenuation coefficient for a photon energy $h\nu$ and the atomic number of the traversed material Z . The total attenuation coefficient is the sum of the attenuation coefficients for the individual photon interactions: σ_R , τ and κ :

$$\mu(h\nu, Z) = \tau(h\nu, Z) + \sigma_R(h\nu, Z) + \kappa(h\nu, Z), \quad (2.2)$$

here τ , σ_R and κ , are the attenuation coefficients of the photoelectric effect, Compton effect, and pair production, respectively [14].

A typical dose distribution of a megavoltage photon beam in water is shown in Figure 2.1. The dose initially increases rapidly until it reaches its maximum value. This region is referred to as the dose build-up region and is caused by the deposition of energy from released secondary electrons through the interactions mentioned earlier. The depth at which the maximum dose occurs is approximately equal to the maximum range of the secondary electrons. Following the maximum dose, the dose decreases exponentially due to the energy-dependent beam attenuation, as described in equation (2.1) [14].

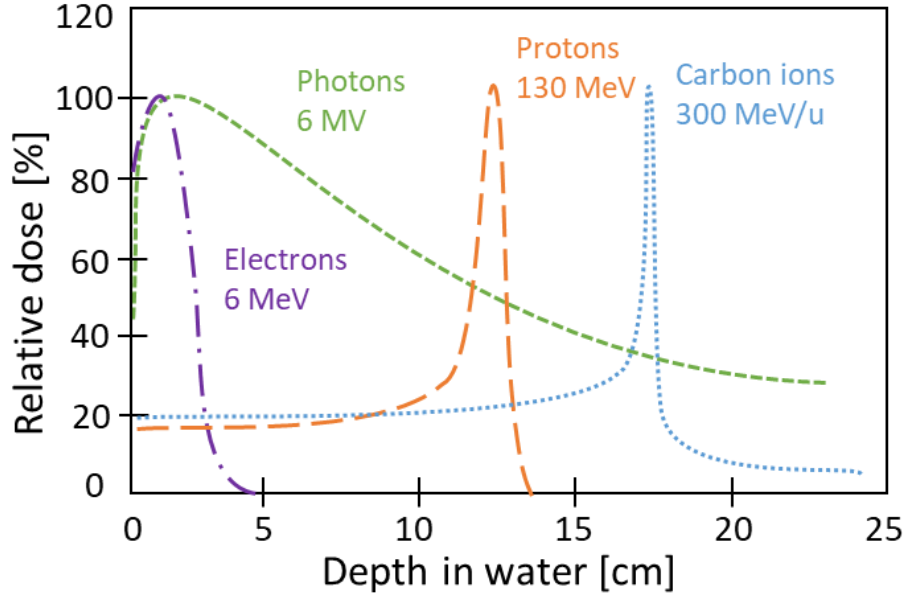


Figure 2.1 Schematic drawing of characteristic relative dose distributions of different particles as a function of depth in water.

2.1.2 Interactions of charged particles

The interactions of charged particles with matter depend on their energy and type, and the properties of the material they traverse. These interactions are relevant for primary charged particles used in radiation therapy but also for the released secondary electrons or, in case of ions, secondary charged particles from nuclear reactions. In this thesis, the focus is on primary carbon-ions as well as the secondary electrons produced from both carbon-ion and photon beams.

Charged particles deposit their energy to matter through Coulomb interactions with orbital electrons or nuclei. Due to the small energy transfer in each interaction, charged particle continues to lose energy gradually as it undergoes a large number of interactions until it finally comes to rest. This process is often referred to as the continuous slowing down approximation (CSDA). The mean energy loss $d\bar{E}$ of a charged particle per unit length dx is described by the linear stopping power S :

$$S = - \left(\frac{d\bar{E}}{dx} \right) = S_{col} + S_{rad} + S_{nuc} . \quad (2.3)$$

It consists of (1) collision (ionization, electronic) S_{col} , (2) radiative S_{rad} and (3) nuclear S_{nuc} components.

The radiative component refers to the energy loss of a charged particle due to the emission of photons, known as Bremsstrahlung, resulting from the deflection of the charged particle from an atomic nucleus. It is only relevant for electrons due to their low mass, whereas it can be neglected for protons and carbon-ions at clinical energies. The nuclear component refers to the energy loss due to elastic Coulomb interaction with an atomic nucleus. This component becomes negligible for energies above 1 MeV, therefore it is only relevant for low energy secondary electrons. The collision stopping power describes the inelastic Coulomb interactions of charged particle with atomic orbital electrons. Both, secondary electrons and ions experience this interaction. For clinically relevant energies of carbon-ions, the S_{col} is the only dominant contribution of the energy loss in tissue. In this interaction, ions transfer the energy to orbital electrons, resulting in excitation or ionization of atoms in the matter [14]. The energy loss of a charged particle with velocity v in a single collision with electron is limited to the maximum energy transfer W_{max} :

$$W_{max} = 2m_e c^2 \frac{\beta^2}{1 - \beta^2}, \quad (2.4)$$

with $\beta = v/c$ as the ratio of velocity and the speed of light and electron mass m_e . The collision energy loss is described mathematically by the well-known Bethe formula [55][56]:

$$S_{col} = \frac{4\pi n_e q^2}{m_e c^2 \beta^2} \left(\frac{e^2}{4\pi \epsilon_0} \right)^2 \left[\ln \left(\frac{W_{max}}{I} \right) - \beta^2 \right], \quad (2.5)$$

Where the electron density of the material is n_e , the incoming particle charge is q , the vacuum permittivity is ϵ_0 and the ionization potential of matter is I .

In the CSDA, the range (or the mean path length) of the charged particle with an initial kinetic energy E_0 can be calculated using the linear stopping power as:

$$R_{CSDA}(E) = \int_0^{E_0} \left(\frac{S(E)}{\rho} \right)^{-1} dE, \quad (2.6)$$

with the density of the traversed material ρ [14].

2.1.3 Electrons in magnetic fields

When secondary electrons produced by the primary radiation pass through magnetic fields, they experience deflection due to the Lorentz force. In a vacuum, when direction of the moving electron is perpendicular to a magnetic field, the Lorentz force leads to a circular trajectory with a radius denoted by r_g (see Figure 2.2). The Lorentz force $\vec{F}_L$ acting on the electrons (in the absence of an electric field) is defined by:

$$\vec{F}_L = -e\vec{v} \times \vec{B}, \quad (2.7)$$

where e represents the elementary charge, $\vec{v}$ the velocity of the electron and $\vec{B}$ the magnetic field. According to this equation, only the velocity component perpendicular to the magnetic field contributes to the Lorentz force. Therefore, if the electron is moving in vacuum at an angle α relative to the magnetic field vector, it will undergo a helical trajectory with a gyromagnetic radius given by:

$$r_g = \frac{\gamma m |\vec{v}| \sin \alpha}{e |\vec{B}|}, \quad (2.8)$$

with the Lorentz factor $\gamma = 1/\sqrt{1 - \beta^2}$. When α is equal to 90° , the trajectory reduces to a circle (Figure 2.2).

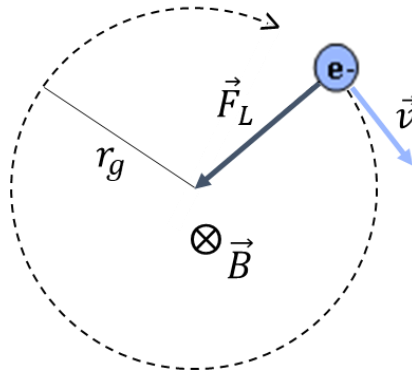


Figure 2.2 Schematic representation of the Lorentz force $\vec{F}_L$ acting on an electron moving in vacuum with a velocity $\vec{v}$ perpendicular to a magnetic field $\vec{B}$.

In media, the trajectory of electrons moving in a magnetic field is influenced by two interactions: the interaction with the medium itself and the interaction with the magnetic field by the Lorentz force. When an electron moves through a medium, it loses energy through various interactions

(as explained in section 2.1.2). As the electron loses energy and its velocity decreases, the circular or helical path described in a vacuum is transformed into a spiral trajectory within the medium (presented in Figure 2.3) [57].

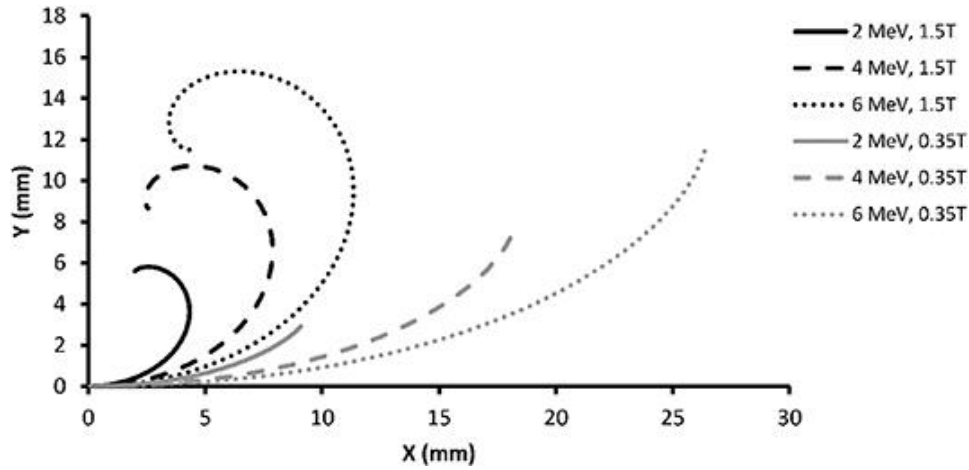


Figure 2.3 Trajectories of electrons at initial kinetic energy of 2, 4 and 6 MeV in a homogenous medium in the presence of a transverse magnetic field with different flux densities of 0.35 T and 1.5 T. Adapted from [57].

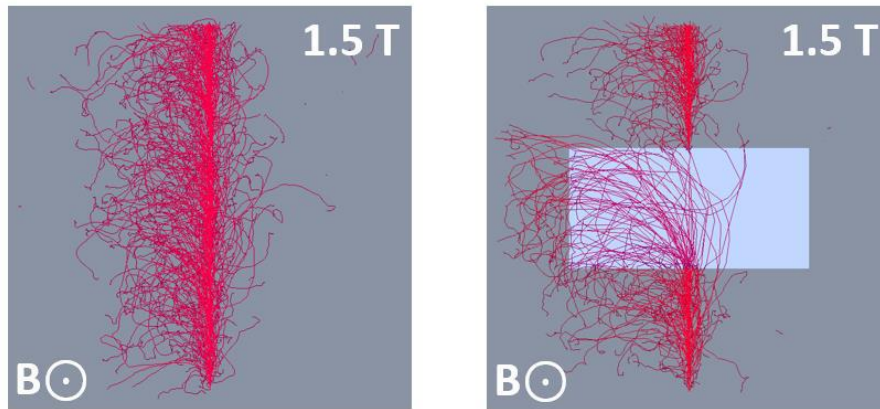


Figure 2.4 Monte Carlo simulation of secondary electron trajectories generated by a 1.2 MeV photon pencil beam in 1.5 T magnetic field: (left) in water and (right) with an air cavity in water. Adopted from [58] with a permission.

The mean free path length of electrons depends on the medium mass density, which has an impact on the gyromagnetic radius (see Figure 2.4). Therefore, when an electron traverses a density inhomogeneous medium, changes in the gyromagnetic radius can occur. Particularly, at

the interface between two regions having different densities, electrons in magnetic fields may experience the so-called electron return effect (ERE) [59]. Here, electrons coming from higher density medium (e.g. water or tissue) and entering a lower density medium (e.g. air) describe a circular path and eventually re-enter the higher density medium under the influence of the magnetic field. This occurs because the the electrons' mean free path is significantly longer in the lower density medium, allowing the circular path to be fulfilled and therefore return the electron to the higher density medium, as presented in Figure 2.5 a [58].

Clinically, this effect can lead to local dose enhancement in higher density medium. For instance, when a photon irradiation is performed in the presence of a perpendicular magnetic field, the ERE can increase the dose at the tissue-air interface by up to 40 % [59]. However, for an ion beam irradiation in magnetic fields, this effect is considerably lower, due to the fact that the secondary electrons generated by the ion beam tend to have lower energies, resulting in much shorter ranges. In the case of proton irradiation in a perpendicular magnetic field, studies have shown an enhancement of up to 10 % at tissue-air interfaces [60].

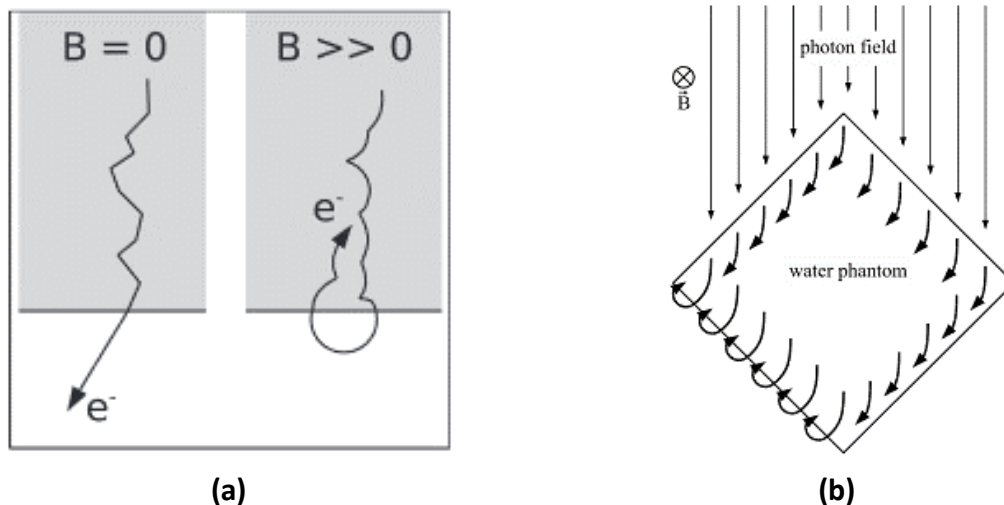


Figure 2.5 Schematic representation of the electron return effect (ERE): (a) at tissue-air interface without and with magnetic field; (b) at the entrance and exit surface of a water phantom in the presence of a magnetic field. Adapted from [61] with a permission.

It is important to note that the magnetic field does not directly affect the photon beam. However, generated secondary electrons experience the Lorentz force, potentially leading to alterations in the dose distribution within the magnetic field. The influence of the magnetic field on the local dose distribution is determined by the magnetic field strength and its orientation with respect to the beam direction, as well as by the energy of the secondary electrons [47].

In the case of ion beam radiation therapy, the Lorentz force acts also on the primary charged particles. As a result, the primary beam may be deflected from its intended path. The literature

reports the displacements in the position of the Bragg peak ranging from a few millimeters up to several centimeters [62]–[64]. However, the curved path of ion beams in a magnetic field is predictable and can be considered during treatment planning.

2.2 Radiation dosimetry

2.2.1 Absorbed dose to water

Accurate dosimetry is crucial to specify the dose delivered to a patient during radiation therapy. A dosimetric protocol aims to measure the dose with the lowest possible uncertainty. To achieve this purpose, radiation detectors used for dosimetric measurements have to be calibrated following a universal protocol and traceability to primary standards [65]. Internationally accepted reference quantity for radiation therapy is the absorbed dose to water D_w . Water is commonly used as a medium for dose determination because it closely resembles the radiation interaction properties of human tissue, allowing for accurate estimation of the dose delivered to the patient. Furthermore, the use of water as a standard medium enables easy comparison of dose measurements across different institutions.

The absorbed dose to water D_w is defined as the mean energy $d\bar{\varepsilon}$ imparted by ionizing radiation to a mass of water dm_w

$$D_w = \frac{d\bar{\varepsilon}}{dm_w}, \quad (2.9)$$

and is measured in units of Gray (Gy), $1 \text{ Gy} = 1 \text{ J/kg}$ [14].

To the date, the most accurate and direct method for determining the absorbed dose to water D_w is water calorimetry, as it enables to measure the quantities in terms of which D_w is defined. In water calorimetry, the energy deposited by the radiation beam is measured as an increase in temperature of a water sample. By accurately measuring the temperature change, the absorbed dose to water can be determined. However, water calorimetry requires special equipment that is not practical for routine clinical measurements [66]. In fact, it is typically performed in Primary Standard Dosimetry Laboratories (PSDL) and serves as a reference method for calibrating detectors used in clinical practice.

2.2.2 Ionization chamber-based dosimetry

In the clinics, the determination of D_w is usually based on measurements with an air-filled ionization chamber placed in a water phantom. Ionization chambers are commonly used detectors due to the fact that they are highly accurate, easy to handle, and affordable.

One type of ionization chamber that is commonly used in the clinics is the thimble chamber, which has a cylindrical design (a simplified schematic is presented in Figure 2.6). The main components of the thimble chamber are the chamber wall, the central (collecting) electrode and the guard electrode. An electric potential is established between the central electrode and the wall of the chamber to create an electric field between them. When the ionizing radiation produces ion pairs, consisting of electrons and positive ions, the electric field separates and pulls them towards the charged electrodes, according to their polarity. The charge Q collected by the electrodes or the current I can be measured by an electrometer. The electric field in the chamber defines the *effective sensitive volume*¹. Improved uniformity of the electric field is also provided by the guard electrode [67]. Positioned at the stem of the chamber, the guard electrode shields the central electrode from any leakage current flowing from the chamber wall. To prevent leakage between the guard electrode and the central electrode, these two electrodes are set at nearly the same potential. However, the guard electrode is not connected to the electrometer. Any variation in the potential of the central electrode relative to its guard electrode can cause distortion in the electric field near the chamber stem (as presented in the Figure 2.5) [68]. This produces a so-called “dead” volume region from which the central electrode is unable to collect the released charges [69]. This effect of the dead volume is often disregarded because it is considered to be relatively insignificant in the absence of magnetic fields.

In terms of Q , the absorbed dose D_{air} to a volume with a mass m_{air} can be calculated as follows:

$$D_{air} = \frac{Q}{m_{air}} \left(\frac{W_{air}}{e} \right) \quad (2.10)$$

where $\left(\frac{W_{air}}{e} \right)$ is the mean energy required for an ion pair production in air per unit charge [70].

However, the main interest is not the dose in the air cavity, but rather the dose in the surrounding medium (water) in the absence of the cavity. To transform the absorbed dose in an air cavity D_{air} to the absorbed dose in water, a cavity theory is applied. The cavity theories, such as Bragg-Gray or Spencer-Attix are valid under specific conditions. The Bragg-Gray theory assumes that the cavity is small in comparison to the range of secondary charged particles produced by ionizing radiation. Therefore, the charged particle fluence, ϕ , in the cavity is the same as in the medium

¹ The term “*effective sensitive volume*” refers to the air volume within the chamber that is involved in measuring absorbed dose. It differs from the “*sensitive volume*”, which includes both the *effective sensitive volume* and the *dead volume*.

(i.e. charged particle fluence is not perturbed by the presence of the cavity) [57]. This condition is known as charged particle equilibrium (CPE) and it is defined as:

$$\vec{\nabla}\varphi = 0 . \quad (2.11)$$

Under this condition, the absorbed dose to water can be derived as:

$$D_w = D_{air} \left(\frac{S_{col}}{\rho} \right)_{w,air} , \quad (2.12)$$

where $\left(\frac{S_{col}}{\rho} \right)_{w,air}$, is the ratio of the mass collision stopping powers of water and air [71]. In practice, however, it is challenging to achieve full CPE, as there is always some degree of fluence perturbation by the ionization chamber. This is accounted for by the use of perturbation correction factors [14].

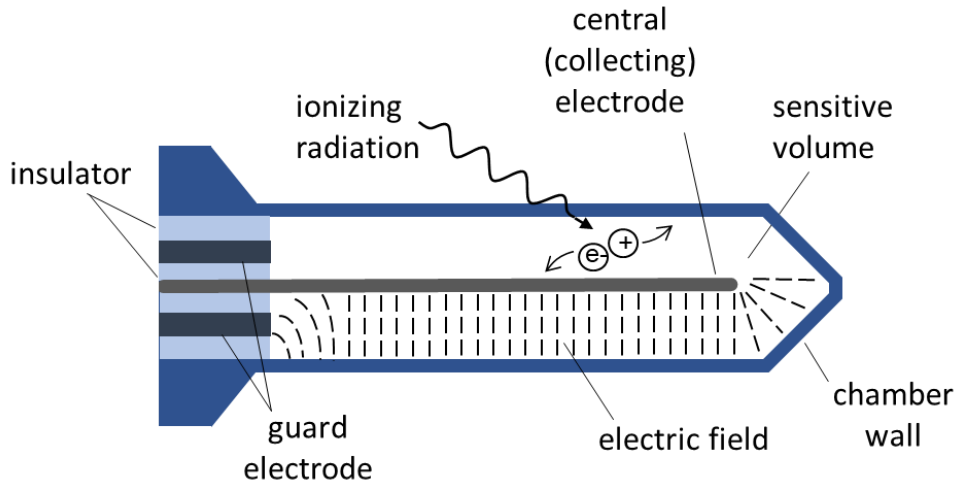


Figure 2.6 Simplified schematic drawing of a cylindrical (thimble) ionization chamber.

Cavity theory provides a mathematical framework for understanding the principle of measuring the absorbed dose with ionization chamber. In practice, however, calibrated ionization chambers are used for absolute dose measurements rather than directly applying cavity theory (equation (2.12)).

2.2.3 Calibration of ionization chambers

Calibration of the chambers provides a relation between the signal of the chamber M and the dose in water at a certain depth in the absence of the chamber. Typically, ionization chambers are calibrated in a Co-60 beam, at the PSDL. After calibration, each chamber is provided with a chamber-specific absorbed dose to water calibration factor N_{D,w,Q_0} , which is the ratio of the true absorbed dose value in water to the signal M_{Q_0} measured under reference conditions in the PSDL. Reference conditions refer to a specific and well-defined set of values (e.g. geometrical arrangement, field size, phantom material, room temperature and air pressure) for which the calibration factor is valid without any further corrections. The absorbed dose to water for a Co-60 reference beam of quality Q_0 in the absence of the chamber is given by:

$$D_{w,Q_0} = M_{Q_0} N_{D,w,Q_0} \cdot \quad (2.13)$$

2.2.4 Clinical dosimetry under reference conditions

Clinical radiation dosimetry can be divided into two categories: reference and relative dosimetry. Reference dosimetry aims to measure the absorbed dose to water under clinical reference conditions at the specific reference point. On the other hand, relative dosimetry determines the dose distribution relative to the reference point. Together, these two categories of dosimetry enable accurate determination of the absolute dose for each measured point.

2.2.4.1 Reference dosimetry according to the protocol TRS-398

The first step in the clinical dosimetry chain is the measurement of the absorbed dose under reference conditions. Reference conditions are described in nationally and internationally adopted protocols for reference dosimetry. Two main international protocols are the International Atomic Energy Agency (IAEA) Code of Practice TRS-398 [41] and the American Association of Physicists in Medicine (AAPM) TG-51 [72]. They are based on measurements with calibrated ionization chambers in terms of absorbed dose to water. While there may be slight differences in the specific requirements and procedures between the protocols, the absorbed dose at a point should be the same, within the uncertainties. Therefore, given the international scope, in the following we will stick to the formalism presented by the TRS-398.

The TRS-398 protocol is intended for the beam qualities used clinically. It is based on chambers calibrated in Co-60 reference beam (beam quality Q_0), with a calibration factor N_{D,w,Q_0} in terms of absorbed dose to water. When the chamber is used in a clinical beam of quality Q , different than reference beam quality Q_0 , radiation beam quality correction factor k_{Q,Q_0} has to be applied.

Following the TRS-398 formalism, when the chamber is positioned according to the reference conditions in a beam of quality Q , the absorbed dose to water is given by:

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0} \quad (2.14)$$

M_Q is chamber reading corrected for influence quantities by the product

$$k = \prod k_i, \quad (2.15)$$

where each correction factor k_i correspond to one influence quantity (e.g. temperature, air pressure, polarity, ion recombination...).

When a chamber is positioned with its cavity center at the reference position z_{ref} , it does not directly sample the electron fluence at that depth in the absence of the chamber as the air cavity reduces the attenuation of the photon beam or shortens the average range of the ion beam. To account for this, the chamber is displaced by an amount that compensates for this effect. The point of the chamber positioned at the reference depth is commonly referred to as the *effective point of measurement*.

All ionization chambers recommended in TRS-398 are vented to the atmosphere, therefore the mass of air in the sensitive volume is affected by the atmospheric variations. When the temperature and pressure differ from the reference values T_0 and p_0 (generally 101.3 kPa and 20° C), chamber reading needs to be corrected by applying $k_{T,p}$ factor:

$$k_{Tp} = \frac{(273.2 + T)}{(273.2 + T_0)} \frac{p_0}{p}. \quad (2.16)$$

The polarity effect on chamber reading is checked by doing measurements with opposing polarizing potentials. For the most chambers this effect is negligible, but when the polarity effect is measurable, it can be accounted for by applying a *polarity correction factor*:

$$k_{pol} = \frac{|M_+| + |M_-|}{2M}, \quad (2.17)$$

i.e. where M_+ and M_- are readings obtained at positive and negative polarity, respectively, and M is the reading obtained with the routinely used polarity (which can be positive or negative).

Due to the recombination of ions in the sensitive volume of the ionization chamber, some of the charge is not properly collected. This effect can be corrected for by applying a *recombination correction factor* k_s calculated by two-voltage method [73]:

$$k_s = \frac{\frac{M_1}{M_2} - 1}{\frac{V_1}{V_2} - 1} + 1, \quad (2.18)$$

where M_1 and M_2 are the collected charges at the voltages V_1 and V_2 , respectively. V_1 is normal operating voltage and V_2 is recommended to be at least three times lower than V_1 . As the two-voltage method assumes linear dependence of $1/M$ versus $1/V$, this condition has to be verified first with the $1/M$ versus $1/V$ curves (Jaffé plots). To produce the Jaffé plot, chamber readings M are measured for different voltages V up to the operational voltage V_1 . If the operating voltage is in the linear region, two-voltage method can be applied for the calculations of k_s .

2.2.4.2 Extension of the protocol TRS-398 to reference dosimetry in presence of magnetic fields

In MRgRT, dosimetry measurements have to be performed in the presence of the permanent magnetic field of the MRI scanner. The magnetic field has the potential to induce alterations in the local dose distribution, and can also influence the response of ionization chambers. However, current dosimetry protocols, such as TRS-398 do not account for magnetic fields for measurements under the reference conditions.

To address the influence of the magnetic field, an additional magnetic field correction factor, denoted as $k_{\vec{B},Q}$ is proposed [43] [47] [45]. For determination of the $k_{\vec{B},Q}$, it is necessary to consider both, the change in the local dose and the change of the chamber reading.

When ionization chambers are used in magnetic fields, several factors come into play that can affect the chamber reading. The electron return effect (ERE), previously explained in the section 2.1.3, can create some hot spots (areas with an excess of charge) and cold spots (areas with a deficit of charge) within the chamber [44] [50]. Additionally, the Lorentz force, can guide the charge carriers towards the dead volume or away from it.

The magnetic field correction factor $k_{\vec{B},Q}$, corrects the chamber calibration coefficient for the influence of the magnetic field. It takes into account the orientation of the magnetic field relative to the beam direction and the chamber itself, therefore, $\vec{B}$ is specified as a vector [57]:

$$D_{w,\vec{B},Q} = M_{\vec{B},Q} N_{D,w,Q_0} k_{Q,Q_0} k_{\vec{B},Q}, \quad (2.19)$$

where $D_{w,\vec{B},Q}$ represents the absorbed dose to water in the magnetic field and $M_{\vec{B},Q}$ is the chamber reading in the magnetic field.

By using equations (2.14) and (2.19) the magnetic field correction factor can be written as:

$$k_{\vec{B},Q} = \frac{D_{w,\vec{B},Q}}{D_{w,Q}} \frac{M_Q}{M_{\vec{B},Q}}. \quad (2.20)$$

The first factor of equation (2.20) represents the ratio of absorbed doses to water with and without magnetic field at the reference point of the chamber, and is denoted by:

$$c_{\vec{B}} = \frac{D_{w,\vec{B},Q}}{D_{w,Q}}. \quad (2.21)$$

To experimentally determine the factor $c_{\vec{B}}$, a dosimeter with response either unaffected by the magnetic field or with a well-known response change in relation to the magnetic field is required. Alanine dosimeters or water calorimeters can be used for this purpose. However, in cases where the magnetic field cannot be switched off, such as in MR-Linacs, it is more practical to calculate this factor using Monte Carlo simulations.

The second factor $k_{\vec{B},M,Q}$ of equation (2.20) represents the ratio of the corrected chamber readings without and with the magnetic field:

$$k_{\vec{B},M,Q} = \frac{M_Q}{M_{\vec{B},Q}}. \quad (2.22)$$

It depends on the magnetic field strength and the orientation of the ionization chamber relative to the magnetic field and beam directions.

Finally, the magnetic field correction factor can be written as the product of the two factors given in equation (2.20) and (2.22):

$$k_{\vec{B},Q} = c_{\vec{B}} k_{\vec{B},M,Q}. \quad (2.23)$$

2.2.5 Relative dosimetry of small photon fields

2.2.5.1 Small field dosimetry according to the protocol TRS-483

In modern radiation therapy, the use of smaller fields and more precise radiation delivery has improved treatment outcome. With image guidance and improved beam delivery techniques, radiation fields, traditionally ranged from (4×4) cm² up to (40×40) cm², have been reduced down to subcentimeter range [15]. Collimating devices such as jaws, MLCs, and cones are used to create small fields of specific shapes and sizes for clinical applications. However, the reduction in field size increased the uncertainty of clinical dosimetry and introduced several dosimetric challenges.

Measurements in small photon fields take place under non-reference conditions and therefore require additional correction factors. Moreover, for technical reasons, devices that produce small fields often cannot replicate the reference conditions (such as a conventional field size of (10×10) cm² as prescribed in protocols for reference dosimetry [74]. This suggests that dosimetry protocols for reference dosimetry, such as TRS-398, may not be applicable to small fields. The need to standardize dosimetry of small fields led to the publication of a new protocol TRS-483 [49], developed by the IAEA and the AAPM. This protocol provides guidelines and recommendations for dosimetry of small photon fields with energies equal to or less than 10 MV, which are commonly used in photon beam radiation therapy. It is specifically designed for measurements with ionization chambers calibrated in terms of absorbed dose to water that are traceable to a PSDL. According to this protocol, a beam is considered small if at least one of the following conditions is met:

- (i) There is a loss of lateral charged particle equilibrium (LCPE) on the beam axis;
- (ii) There is partial occlusion of the primary source by the collimating devices on the beam axis;
- (iii) The size of the detector is similar-sized or larger compared to the beam dimensions (at the depth of measurement).

Small fields have dimensions smaller than the lateral range of charged particles that contribute to the dose. This leads to the loss of LCPE on the central axis (CAX) of the beam, which results in a steep drop in the measured beam output (see Figure 2.7 (i)). The effect of primary photon source occlusion by collimators also leads to changes in the beam spectrum, causing beam hardening and steep dose gradients (see Figure 2.7 (ii)). Choosing a suitable detector for small field dosimetry is challenging due to the volume averaging effect. When the field size is small, the inhomogeneous dose distribution over the detector's sensitive volume causes a lower detector response at the beam axis and a higher response beyond the field edge (Figure 2.7 (iii)). Various detector types have been suggested (e.g. small ionization chambers, microdiamond detectors, silicon diodes, thermoluminescent dosimeters and radiochromic films); however, there is no ideal detector for small field measurements.

In small field dosimetry, as in reference dosimetry, it is essential that all dosimetric measurements are traceable to primary dosimetric standards. This traceability is achieved through a calibration chain, which represents the whole path between a clinical measurement and a standard. If the machine cannot establish the conventional (10 x 10) cm² reference field, with the required source surface/detector distance (SSD/SDD), a machine-specific reference field f_{msr} with a beam quality Q_{msr} is used as a reference. The size of the reference field and the distances may vary depending on the type of machine, but it should be as close as possible to the conventional reference conditions. The use of the calibration coefficient in a beam of a different quality than the one used for chamber calibration requires the application of a beam quality correction factor $k_{Q_{msr}, Q_0}^{f_{msr}, f_{ref}}$, similarly to the equation (2.14) for the broad fields.

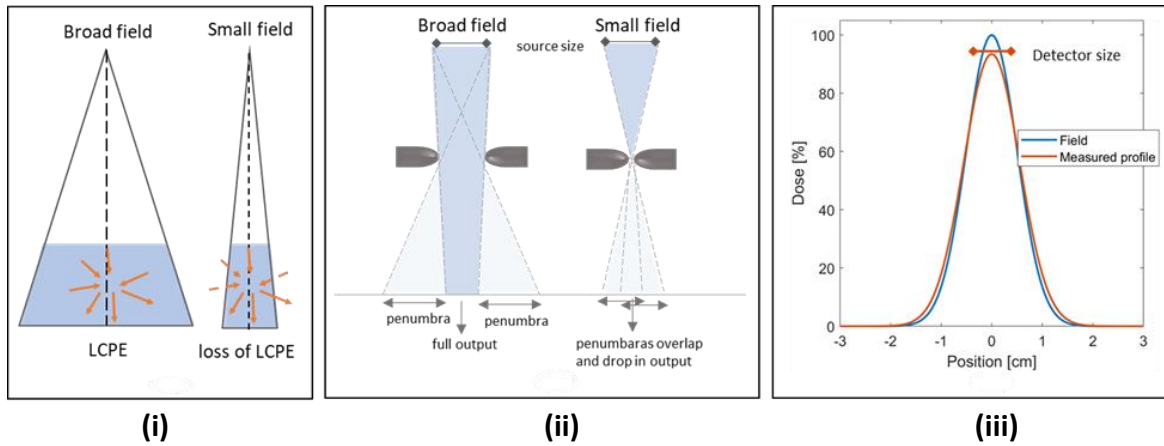


Figure 2.7 The physical conditions of the small fields: (i) Loss of LCPE; (ii) Partial source occlusion of the primary radiation source by collimating devices; (iii) Volume averaging effect that occurs when the detector size is large compared with the radiation field size.

Therefore, the absorbed dose to water in the f_{msr} is:

$$D_{w,Q_{msr}}^{f_{msr}} = M_{Q_{msr}}^{f_{msr}} N_{D,w,Q_0}^{f_{ref}} k_{Q_{msr},Q_0}^{f_{msr},f_{ref}}. \quad (2.24)$$

As dosimetry of small photon fields deviate in many aspects from broad reference dosimetry, the TRS-483 formalism uses an output correction factor $k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$ to correct the detector calibration coefficient in a f_{msr} with beam quality Q_{msr} to one for a small clinical field f_{clin} with beam quality Q_{clin} . Therefore, the absorbed dose to water for the small clinical field f_{clin} is given by:

$$D_{w,Q_{clin}}^{f_{clin}} = M_{Q_{clin}}^{f_{clin}} N_{D,w,Q_0}^{f_{ref}} k_{Q_{msr},Q_0}^{f_{msr},f_{ref}} k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}, \quad (2.25)$$

where $M_{Q_{clin}}^{f_{clin}}$ is the reading of the chamber in the small clinical field corrected for influence quantities (see the equation (2.15)).

To convert absorbed dose to water for the machine-specific reference field f_{msr} and beam quality Q_{msr} to the absorbed dose to water for the clinical field f_{clin} with beam quality Q_{clin} the field output factors are used. The field output factor is defined as the ratio of absorbed doses to water in the clinical small field to machine-specific reference field:

$$\Omega_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} = \frac{D_{w,Q_{clin}}^{f_{clin}}}{D_{w,Q_{msr}}^{f_{msr}}}. \quad (2.26)$$

The field output factor can be derived from a ratio of detector readings (output factor²) by multiplying it by an output correction factor $k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$:

$$\Omega_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} = \frac{M_{Q_{clin}}^{f_{clin}}}{M_{Q_{msr}}^{f_{msr}}} k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}. \quad (2.27)$$

Only when the detector reading is directly proportional to absorbed dose to water, the output correction factor reaches unity and field output factor becomes equal to the ratio of detector readings. The output correction factors might be very near to unity for some very small detectors with an energy independent response, like radiochromic film, a liquid ionization chamber, or an organic scintillator. However, measurements with multiple detectors are recommended to obtain field output factors [49].

² The term “output factor” represents the ratio of dosimeter readings, which has to be distinguished from “field output factor” which is the ratio of doses.

The small square field sizes are defined by the full width at half maximum (FWHM) of the perpendicular lateral beam profiles. FWHM represents the distance between the points on the lateral profile where the dose is at 50 % of the relative dose level. The TRS-483 protocol provides detector-specific output correction factors as a function of the equivalent square field size. For non-square fields, the geometric mean formula is proposed to determine the equivalent square small field size:

$$S_{eq} = \sqrt{XY}, \quad (2.28)$$

where X and Y are cross-plane and in-plane FWHMs. This formula should not be used for FWHMs outside the condition $0.7 < X/Y < 1.4$, otherwise, the output correction factors calculated based on S_{eq} must be considered with larger uncertainty [49]. It is important to highlight that the formula for equivalent square small field size determination is different from the formula applied for broad beams [14]:

$$S_{eq} = \frac{2XY}{X + Y}. \quad (2.29)$$

2.2.5.2 Extension of the protocol TRS-483 to small field dosimetry in presence of magnetic fields

The protocol for traceable small field dosimetry TRS-483 has not yet addressed the application in magnetic fields. However, small fields are often used in MRgRT and, therefore, dosimetry of this kind of fields has to be performed in the presence of magnetic fields. This protocol extension for small fields in magnetic fields was a result of the collaborative MRgRT-DOS project [53], although the deliverables are still not publicly available.

Ionization chambers used in MRgRT are typically calibrated at a standard laboratory in a Co-60 beam of quality Q_0 in a conventional (10×10) cm² reference field f_{ref} in absence of magnetic fields. The formalism to extend the TRS-483 to small field dosimetry in the presence of magnetic fields is schematically illustrated in Figure 2.8. Following this formalism, the absorbed dose to water for in the machine-specific reference field $D_{w,\vec{B},Q_{msr}}^{f_{msr}}$ can be derived by measuring the chamber response in magnetic fields $M_{\vec{B},Q_{clin}}^{f_{clin}}$ and incorporating an additional magnetic field correction factor $k_{\vec{B},Q_{msr}}^{f_{msr}}$ to the equation:

$$D_{w,\vec{B},Q_{msr}}^{f_{msr}} = M_{\vec{B},Q_{msr}}^{f_{msr}} N_{D,w,Q_0}^{f_{ref}} k_{Q_{msr},Q_0}^{f_{msr},f_{ref}} k_{\vec{B},Q_{msr}}^{f_{msr}}. \quad (2.30)$$

Similarly, the dose to water for the small clinical field f_{clin} in the presence of magnetic field $D_{w,\vec{B},Q_{clin}}^{f_{clin}}$ is obtained by applying $k_{\vec{B},Q_{clin}}^{f_{clin}}$ to the equation (2.25):

$$D_{w,\vec{B},Q_{clin}}^{f_{clin}} = M_{Q_{clin}}^{f_{clin}} N_{D,w,Q_0}^{f_{ref}} k_{Q_{msr},Q_0}^{f_{msr},f_{ref}} k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} k_{\vec{B},Q_{clin}}^{f_{clin}}, \quad (2.31)$$

where $M_{\vec{B},Q_{clin}}^{f_{clin}}$ is the corrected chamber readings in the presence of magnetic field for the small clinical field. The field output factor in magnetic field is the ratio of absorbed doses in the magnetic field:

$$\Omega_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} = \frac{D_{w,\vec{B},Q_{clin}}^{f_{clin}}}{D_{w,\vec{B},Q_{msr}}^{f_{msr}}}. \quad (2.32)$$

Replacing the $D_{w,\vec{B},Q_{clin}}^{f_{clin}}$ with equation (2.30) and $D_{w,\vec{B},Q_{msr}}^{f_{msr}}$ with equation (2.31) leads to:

$$\Omega_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} = \frac{M_{\vec{B},Q_{clin}}^{f_{clin}}}{M_{\vec{B},Q_{msr}}^{f_{msr}}} k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} \frac{k_{\vec{B},Q_{clin}}^{f_{clin}}}{k_{\vec{B},Q_{msr}}^{f_{msr}}}. \quad (2.33)$$

Finally, the field output factor in magnetic field can be written as:

$$\Omega_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} = \frac{D_{w,\vec{B},Q_{clin}}^{f_{clin}}}{D_{w,\vec{B},Q_{msr}}^{f_{msr}}} = \frac{M_{\vec{B},Q_{clin}}^{f_{clin}}}{M_{\vec{B},Q_{msr}}^{f_{msr}}} k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}, \quad (2.34)$$

with the *output correction factor* in the presence of a magnetic field $k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$ given by:

$$k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} = k_{Q_{clin},Q_{msr}}^{f_{clin},f_{msr}} \frac{k_{\vec{B},Q_{clin}}^{f_{clin}}}{k_{\vec{B},Q_{msr}}^{f_{msr}}}. \quad (2.35)$$

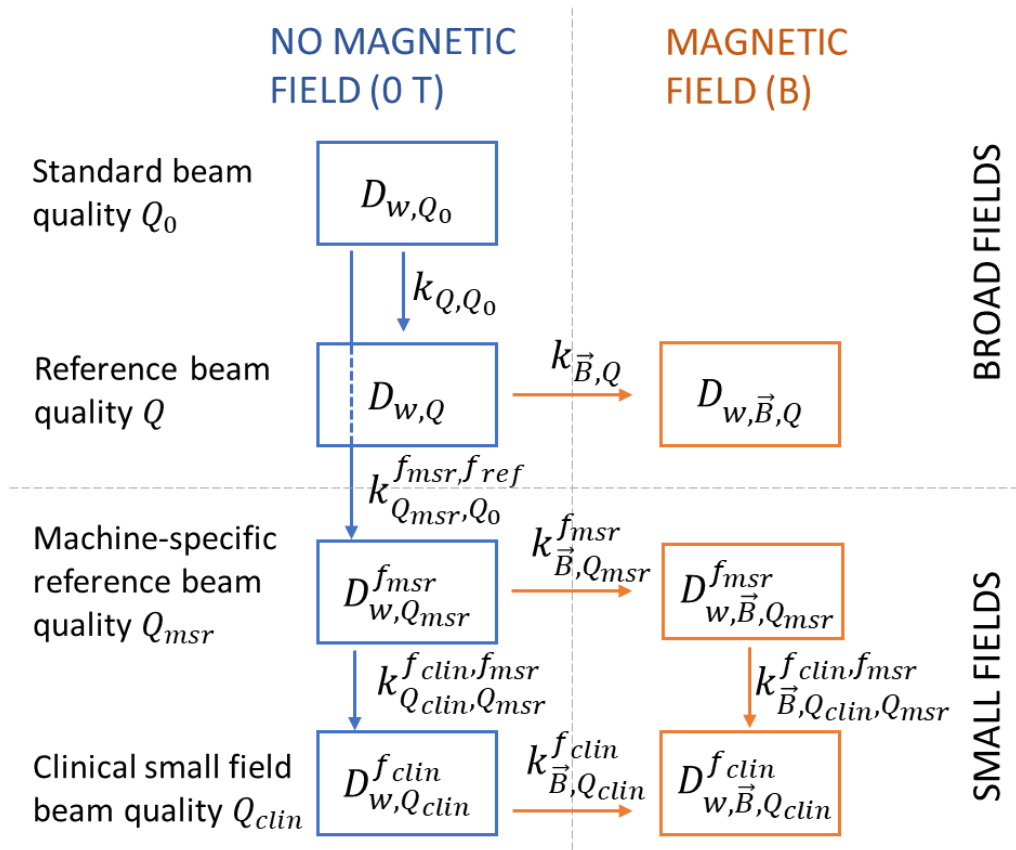


Figure 2.8 Schematic illustration of the formalism for broad and small fields with and without applied magnetic fields. Correction factors represent the connections in the dosimetric chain.

Relative dosimetry in small fields involve three different types of measurements: percentage depth dose (PDD), lateral profiles, and output factors. These measurements help characterize the dose distribution and output of radiation beams.

Percentage depth dose

Percentage depth dose (PDD) characterizes the distribution of the dose along the depth. The PDDs are commonly measured in a water phantom at the center of the beam. The measured dose values obtained at different depths are then normalized to the maximum. The PDD increases from the water surface to the depth of the maximum dose and decreases exponentially beyond the depth of maximum dose, as explained in section 2. Initial dose increase is explained by long-ranging electrons that are ejected from the water surface and deposit their energy away from their origin [66].

In a magnetic field perpendicular to the beam, the curved path of the electrons causes a dose reduction and a shift of the PDD curve towards shallower depths. For small fields, this effect is more pronounced (see Figure 2.9 (b)).

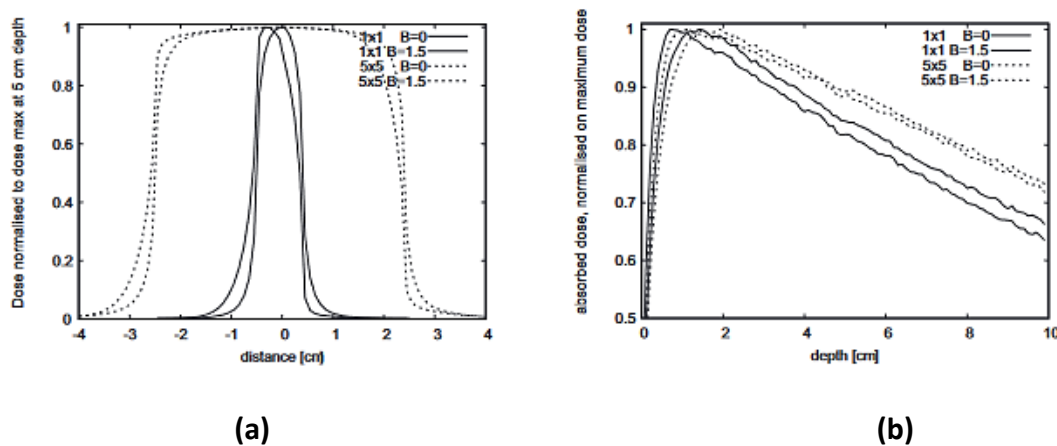


Figure 2.9 Comparison of the Monte Carlo simulated (a) lateral beam profiles and (b) depth-dose curves (PDDs) with and without a 1.5 T perpendicular magnetic field for a small field (solid line) and a large field (dashed line). Reproduced with permission from [61].

Lateral beam profiles

Lateral beam profiles present the dose variation along a line perpendicular to the CAX at a certain depth. The measured dose values are normalized to the maximum. Typically, lateral profiles are measured in two orthogonal directions known as inline and crossline profiles. By examining the shape and characteristics of the profiles, the symmetry of the beam and the field size can be determined (as explained in section 2.2.5).

In a magnetic field perpendicular to the beam, lateral profiles become asymmetric with a tilt in the direction of the Lorentz force. For small fields, a lateral shift of the dose maximum can be observed in addition to the asymmetry of the profile shape (see Figure 2.9 (a)).

Output factors

Output factors represent the ratio of detector readings between a small and the reference field

$\frac{M_{Q_{clin}}^{f_{clin}}}{M_{Q_{msr}}^{f_{msr}}}$. In MRgRT, this ratio is measured in the presence of the static magnetic field $\vec{B}$, $\frac{M_{\vec{B},Q_{clin}}^{f_{clin}}}{M_{\vec{B},Q_{msr}}^{f_{msr}}}$. In

order to calculate the field output factor, this ratio has to be multiplied by the output correction factor $k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$ (see equation (2.34)).

2.3 Experiments

2.3.1 Carbon-ion reference dosimetry in magnetic fields

2.3.1.1 Experimental setup

The following section describes the experimental setup used for chamber measurements in magnetic fields. The responses of six ionization chambers of varying inner radii (1 to 6 mm, termed as R1 to R6) to a monoenergetic carbon-ion beam were measured in magnetic fields of an experimental electromagnet.

The R3 chamber is the commercially available Farmer chamber (type TM30013, PTW, Freiburg, Germany), while the other chambers (type TM30013-1, TM30013-2, TM30013-4, TM30013-5, TM30013-6) are custom-made. All chambers are built of the same material, contain the same aluminium central electrode, and a cavity length of 23 mm, thus only the radius varies (see Figure 2.10). Previously, the response of these chambers to photon beams without [75] and with magnetic fields [44], as well as protons in magnetic fields [50], had been examined using a similar experimental setup.

To generate magnetic fields, an electromagnet (AGEM 5520, Schwarzbeck Mess - Elektronik, Germany) with a variable air gap between the magnet poles was used. To achieve magnetic flux densities of up to 1 T, the gap was set to 3.5 cm. The magnetic flux density was controlled by remotely changing the current in the electromagnet. To avoid systematic effects in the measured data due to magnetic hysteresis effect, each set of magnetic flux densities ranging from 0.1 to 1.0 T was randomized.

A small water phantom with size of (12 x 3.5 x 10) cm³ was fixed between the poles of the electromagnet. The phantom was designed in-house and 3D printed with water-equivalent printing material (Vero Clear, Stratasys, USA). The central axis of the chamber was placed in the phantom at 20 mm water-equivalent depth using a chamber-specific holder. The chamber orientation was perpendicular to the beam as well as to the magnetic field (see Figure 2.11 (a)).

Since the response of the chamber depends on the temperature via the air density, it was important to avoid an increase of the water temperature due to the heating of the magnet coils. This was achieved (i) through a ribbed contact surface between the phantom and the pole shoes, and (ii) through an integrated water circulation system that exchanged the water in the phantom with thermalized water from a 20-liter water canister. These measures together with short irradiation times and breaks between measurements limited the temperature variations to less than 0.3 °C. The remaining variations were temperature corrected by taking the average reading from two thermometers (TFA Dostmann GmbH & Co. KG, Germany) placed at the inflow and outflow of the water phantom.

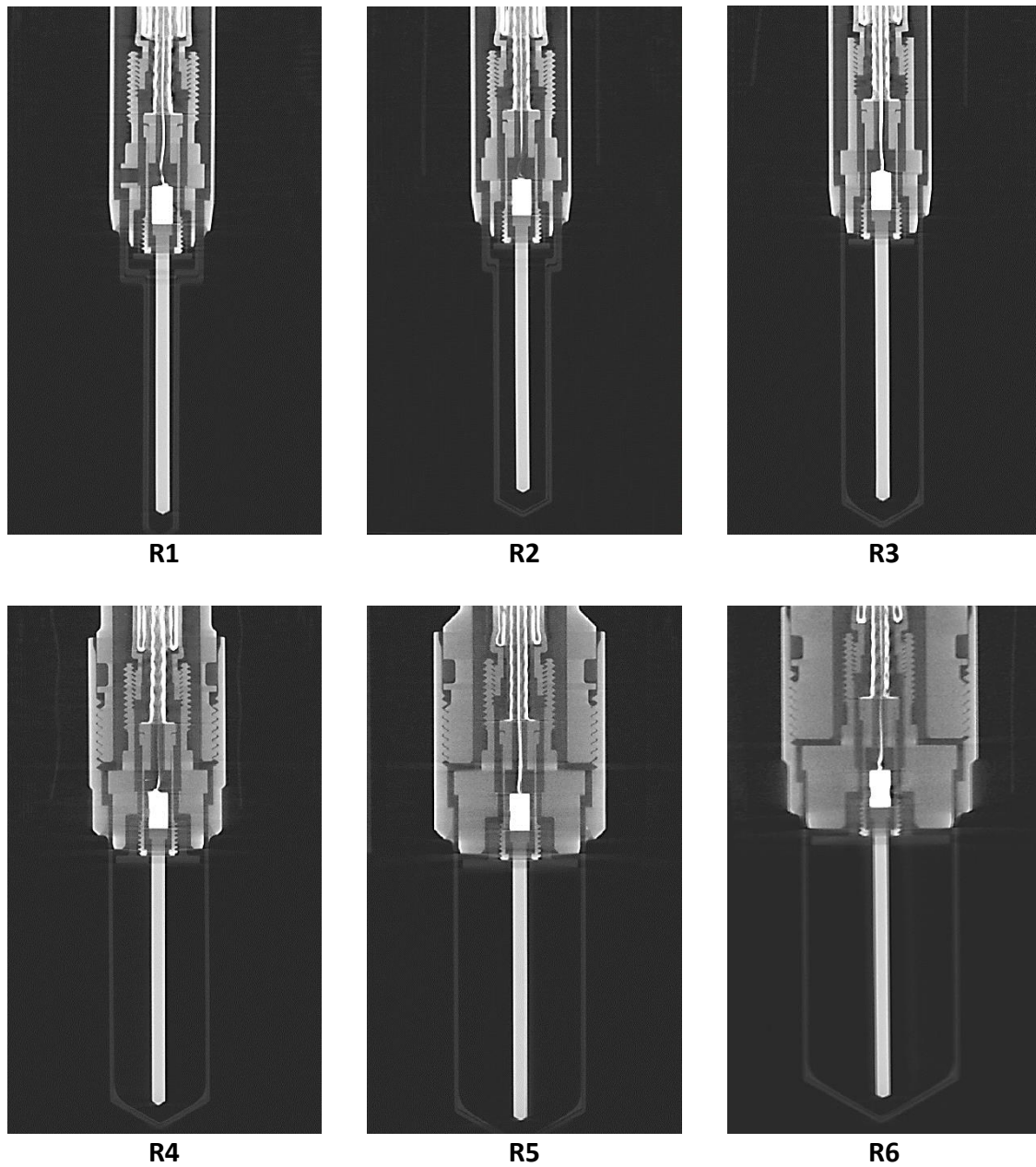


Figure 2.10 μ CT of six Farmer-type ionization chambers of varying inner radii. R1 exhibits a slight bending of the central electrode.

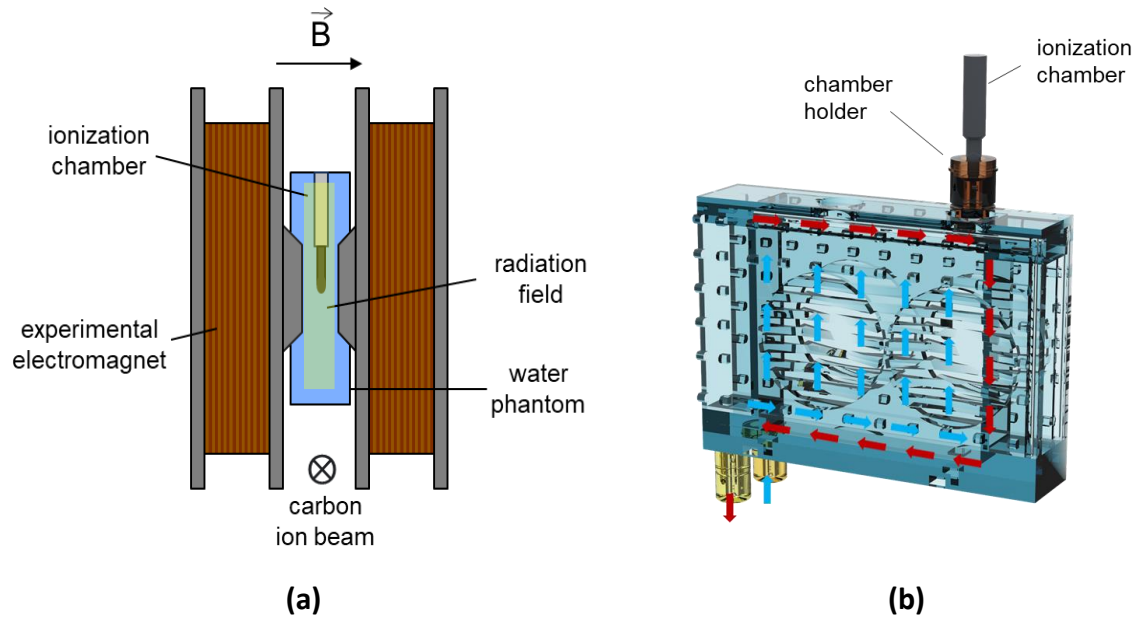


Figure 2.11 Schematic drawing of (a) the experimental setup; and (b) the water phantom with integrated water circulating system. The blue arrows represent the inlet and red arrows the outlet path of the water.

2.3.1.2 Measurements

The measurements were performed using a monoenergetic horizontal carbon-ion beam with an energy of 390.75 MeV/u at the experimental beamline of the Heidelberg Ion Beam Therapy Center (HIT) [76]. For the R3 chamber, an additional lower energy of 200.28 MeV/u was used for comparison. The position of the chamber corresponded to the entrance region of the Bragg-peak. The lateral field size was limited by the distance of the pole shoes of the electromagnet in order to avoid backscattering from the magnet. Therefore, the recommended (10 x 10) cm² reference field size was reduced to (3 x 10) cm². The field was created by superposition of 816 pencil beams with 2 mm spacing and the FWHM of 7.9 mm.

Each chamber was measured on three different days, with at least three measurements per day resulting in 9-27 measurements per chamber and magnetic flux density. The dose per measurement was 0.25 Gy, and no repositioning of the chamber was performed during the measurement day. The chambers were pre-irradiated with 5 Gy using the same energy to obtain stable readings, and the chamber signal was read out using an Unidos electrometer from PTW in Freiburg, Germany.

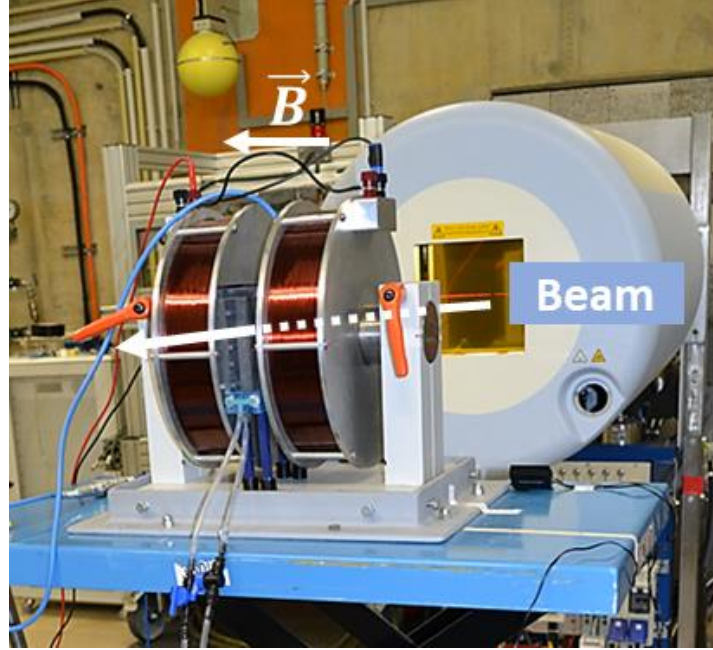


Figure 2.12 The experimental setup at the Heidelberg Ion Beam Therapy Center (HIT).

2.3.1.3 Polarity and ion recombination correction

In order to account for dosimetric influence quantities caused by the polarity of the voltage and ion recombination on the chamber reading, investigation of the polarity k_{pol} and ion recombination k_s corrections was performed. In this study, the impact of magnetic fields on k_{pol} and k_s was investigated for the commercially available PTW 30013 ionization chamber (R3). For this, the R3 chamber was irradiated with a mono-energetic carbon-ion beam with an energy of 390.75 MeV/u, and k_{pol} and k_s correction factors were calculated for magnetic flux densities of 0 T, 0.2 T, 0.3 T, and 1 T.

The polarity correction factor k_{pol} was calculated by measuring the R3 chamber reading at opposing polarizing potentials (- 400 V and + 400 V) and applying the equation (2.17).

The ion recombination correction factor k_s for R3 chamber was calculated using the two-voltage method (equation (2.18)) by setting the voltage V_1 at 400 V and voltage V_2 to 50 V. The two-voltage method requires linear dependence of $1/M$ and $1/V$ (Jaffé-plot). This condition was verified by measuring the chamber readings at 50 V, 100 V, 200 V, 300 V, and 400 V.

2.3.1.4 Chamber response in magnetic fields

The comparison of chamber readings in the absence (M_Q) and presence ($M_{\vec{B},Q}$) of a magnetic field was performed to determine the $k_{\vec{B},M,Q}$ factor (see equation (2.22)).

The experiments were performed with six ionization chambers (R1-R6) and for ten magnetic flux densities (0.1 T - 1 T in steps of 0.1 T). The $k_{\vec{B},M,Q}$ factor was calculated for each chamber and magnetic flux density. Each chamber reading was corrected for temperature and pressure according to the TRS-398 (see equation (2.16)). The same-day chamber readings were always used to calculate the $k_{\vec{B},M,Q}$ factor to ensure consistency in the experimental setup. The experiments were repeated on different days, and the final $k_{\vec{B},M,Q}$ value was calculated as the mean of the $k_{\vec{B},M,Q}$ values obtained from each day. The final standard error of the mean for $k_{\vec{B},M,Q}$ factor was calculated using the inverse-variance weighted method to consider the variance of each measurement and weight them accordingly.

To assess if the charge collection in the chamber was significantly different with and without a magnetic field, the two-sided Student's t-test was employed. Prior to conducting the t-test, two prerequisites were evaluated: normality and variance homogeneity. The Shapiro-Wilk test was used to assess normality, while Levene's test was used to examine variance homogeneity. A significance level of 5 % was applied for all the tests.

2.3.2 Small photon field dosimetry in magnetic fields

Measurements were performed at a clinical MR-Linac and included *scanning* and *point measurements*, as shown in Figure 2.13. Scanning measurements involved moving the dosimeter in the water phantom in different directions. Specifically, by scanning the lateral dose distribution at a specific depth, the position and the width (FWHM) of the mean was determined. In PDD measurements, the dosimeter was moved along the depth of the water in longitudinal direction of the beam. This measurement allows for the evaluation of the dose distribution as a function of depth.

Unlike scanning measurements, point measurements involved assessing the radiation at specific points. In the case of small fields, monitoring the output variations of the MR-Linac was not feasible. Therefore, investigation of the chamber reading for different number of monitor units (MU) was performed. Additionally, the influence factors on the chamber reading for small fields were examined. This investigation included measurements of polarity and ion recombination correction factors. Finally, measurements of the output factors were performed.

Lateral profiles, PDDs and output factors were measured for various small fields as well as the machine-specific reference field. Small fields included *square isocentric*³ fields, *rectangular isocentric* fields and *square off-axis*⁴ fields.

³ *Isocentric fields (or on-axis)*: radiation fields for which the central beam axis coincides with the machine isocenter.

⁴ *Off-axis fields*: radiation fields for which the central beam axis is shifted relative to the machine isocenter.

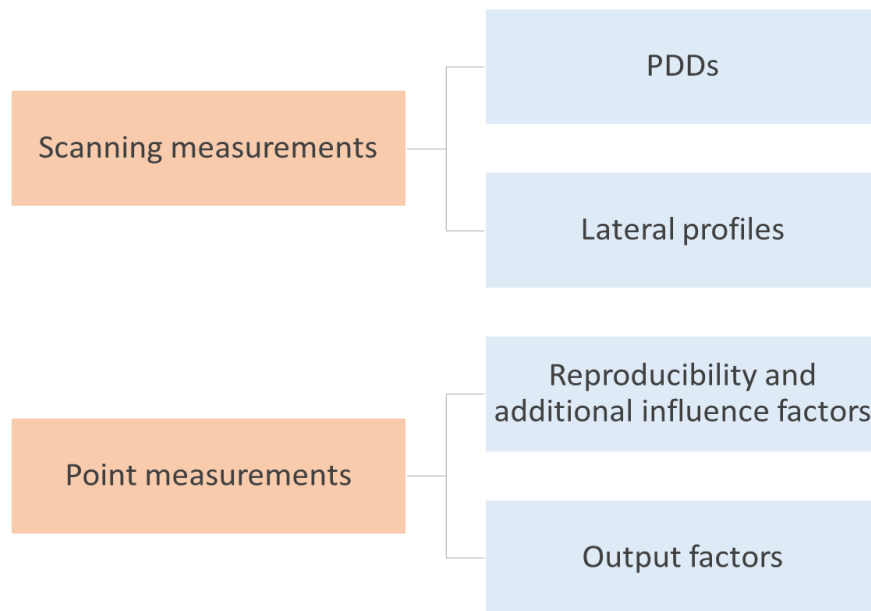


Figure 2.13 Schematic illustration of the measurements performed at MR-Linac: Scanning measurements include: measurements of the percentage depth dose curves (PDDs) and measurements of the lateral beam profiles (X – cross-plane profile, and Y – in-plane profile). Point measurements, include: measurements of reproducibility and additional influence factors and measurements of output factors.

2.3.2.1 Experimental setup

The experiments were performed at a 6 MV flattening-filter-free (FFF) photon beam of the MRIdian MR-Linac (ViewRay Inc., Oakwood, USA) at the Heidelberg University Hospital. A detailed description of this device has been provided previously [32]. The MRIdian operates with the magnetic field perpendicular to the beam and a magnetic flux density of 0.35 T (refer to Figure 2.14). The ring gantry is positioned between split superconducting magnets. The shared isocenter between the MRI and the Linac gantry is located inside the MRI bore, 90 cm away from the radiation source, known as the source-to-axis distance (SAD). For easier alignment, room lasers project a virtual isocenter outside the bore. The actual isocenter is then reached by moving the couch 155 cm in Y direction. The beam is shaped by double-stacked MLC oriented in the X direction, producing a minimum available nominal field size of $(0.2 \times 0.415) \text{ cm}^2$, and a maximum nominal field size of $(27.4 \times 24.1) \text{ cm}^2$ [32]. All measurements were performed with the Linac gantry angle set to 0° . The equipment used for measurements at MR-Linac was deemed safe for use in the MRI environment.

Measurements were conducted using the MR-compatible scanning water phantom BEAMSCAN MR (PTW, Freiburg, Germany). The BEAMSCAN MR system consists of a PMMA tank with a capacity of 71 liters, a built-in electrometer and a scanning mechanism that enables the detectors to be positioned appropriately for measurements. The scanning mechanism can accommodate two detectors simultaneously, allowing a wider range of measurement positions within the limited space of the bore. Additionally, a reference detector can be attached to the tank at a fixed position within the field to account for changes in the output of the Linac (see Figure 2.9 (b)). The phantom was initially positioned at the virtual isocenter based on laser alignment, as shown in Figure 2.16. Subsequently, the phantom was shifted to the real isocenter, and an additional alignment procedure was performed remotely using the BEAMSCAN software. This procedure involved leveling the phantom to determine the inclination angle. Lateral profile measurements were then carried out with the Linac gantry angle set to 0° and 270° to correct for any offset and rotation of the coordinate system in relation to the radiation field. To ensure accurate positioning of the various detectors at the effective point of measurement, a mounting system with detector-specific TRUFIX holders (PTW, Freiburg, Germany) was used. The positioning of the detector and water level in the tank can be controlled remotely through the BEAMSCAN software.

Two different types of detectors, the PTW PinPoint 3D (31022) ionization chamber and the PTW microDiamond (60019) detector, were used for the measurements. These detectors are suitable for measuring in small fields due to their small sensitive volumes (0.016 cm^3 for the PinPoint 3D chamber and 0.004 mm^3 for the microDiamond detector).

The PinPoint 3D chamber was oriented perpendicular to the beam and parallel to the magnetic field direction, while the microDiamond detector was oriented parallel to the beam and perpendicular to the magnetic field direction (refer to Figure 2.15).

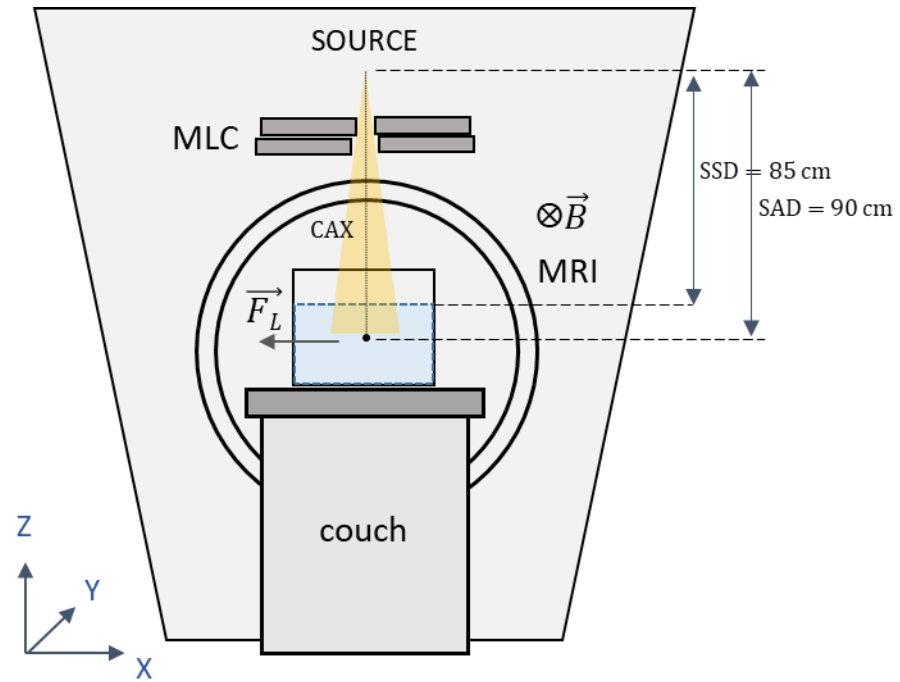


Figure 2.14 Schematic drawing of the measurement setup: water phantom with detector positioned on the couch of the MR-linac machine. Orientation of the beam, magnetic field direction and Lorentz force acting on electrons are indicated.

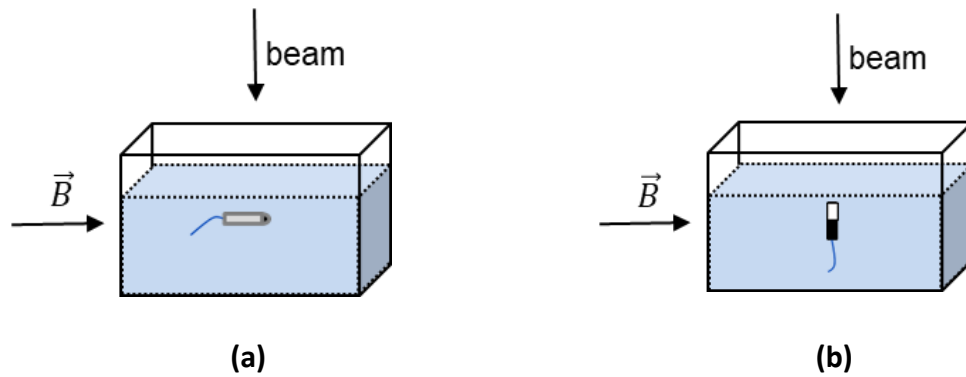


Figure 2.15 Orientation of the detectors used for measurements: (a) PinPoint 3D chamber oriented perpendicular to the beam and parallel to the magnetic field direction; (b) microDiamond detector oriented parallel to the beam and perpendicular to the magnetic field direction.

To monitor output variations, the PTW Semiflex 3D (31021) thimble chamber was used as the reference detector for field sizes larger than $(4 \times 4) \text{ cm}^2$, while the PTW T-REF (34091) transmission chamber was used for field sizes smaller than $(4 \times 4) \text{ cm}^2$. The Semiflex 3D chamber was positioned in the corner of the field, away from the scan path of the detector being used for measurement. In contrast, the T-REF chamber is a thin plane-parallel chamber with a large sensitive volume (diameter of 8.16 cm), which was positioned above the measurement detector at the center of the beam. The monitor signal of these chambers was used to correct for output variations of the MR-Linac in the scanning measurements.

The readout for scanning measurements was performed using the integrated electrometer of the BEAMSCAN MR system. However, for point measurements the Unidos electrometer (PTW, Freiburg, Germany) was used.

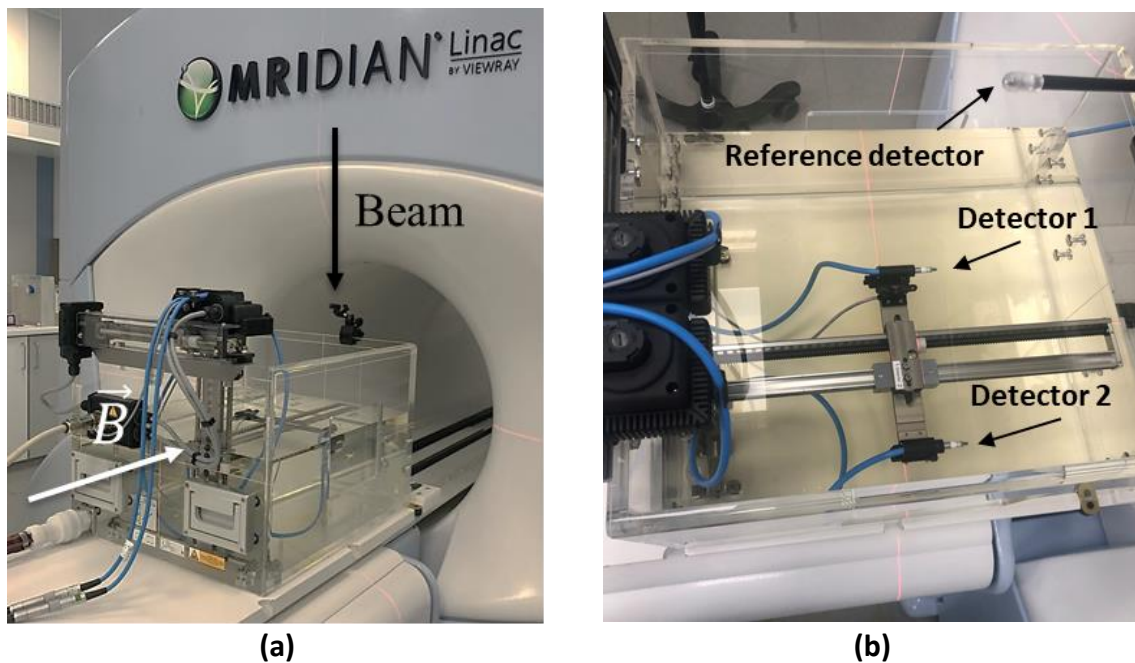


Figure 2.16 BEAMSCAN MR water phantom positioned at the virtual isocenter of MRIdian MR-Linac: (a) side view of the experimental setup; (b) top view of the experimental setup – two PinPoint 3D detectors mounted on the moving arm and Semiflex 3D reference detector attached to the water phantom.

2.3.2.2 Scanning measurements

PDDs for isocentric fields were measured along the CAX by shifting the detector step-wise from 100 mm depth up to the surface, in 1mm steps, while SSD = 85 cm remained fixed. PDDs for off-axis fields were measured by shifting the detector diagonally from the center of the off-axis field to the maximum position of the respective field (see Figure 2.17).

The lateral beam profiles were obtained by moving the detector in both the X and Y directions at SAD = 90 cm and SSD = 85 cm. The scanning steps for the profiles were adjusted based on the field size and the region of interest, with smaller steps used for smaller fields and for the penumbra region. For the cross-plane X profile, two detectors of the same type were positioned on opposite sides of the horizontal scanning arm (see Figure 2.16). This arrangement enabled an extended scan length in the X direction, overcoming the limitation imposed by the MRI bore. The final profile was created by combining the profiles obtained from the two detectors, effectively stitching them together.

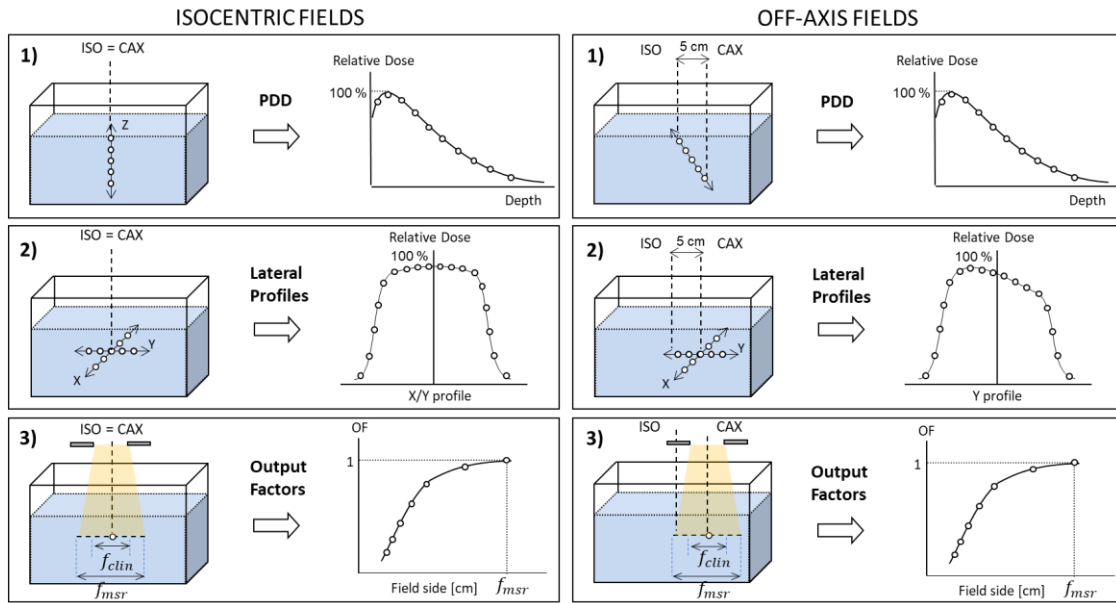


Figure 2.17 Measurements for isocentric and off-axis fields: 1) PDDs obtained by moving the detector in vertical (Z) direction for isocentric fields and in diagonal direction for off-axis fields; 2) Lateral X and Y profiles obtained by moving the detector in X and Y direction, respectively; 3) Output factor measurements obtained by changing the field size from small f_{clin} to the machine-specific reference field size f_{msr} while the detector remains at the same position.

2.3.2.3 Point measurements

All point measurements were conducted with detectors positioned in a water phantom at SSD = 85 cm and SAD = 90 cm.

In order to investigate the output variations of the MRIdian machine for the small fields, measurements of the PinPoint 3D chamber reading were measured for (10, 25, 50, 75, 100, 200, 300 and 500) MU, using a nominal field size of (1.66×1.66) cm². These measurements were repeated three times per setting and on three different days. Polarity and ion recombination effects on reading of PinPoint 3D chamber were investigated for a nominal f_{msr} size of (9.96×9.96) cm² and for the small field with nominal size of (1.66×1.66) cm². The polarity correction factor was calculated by measuring the chamber reading at opposing polarizing potentials (- 300 V and + 300 V) and applying the equation (2.17).

Recombination correction factor was calculated using the two-voltage method (equation (2.18)) by setting the voltage V_1 at 300 V and voltage V_2 to 100 V. The condition of linearity of the Jaffé-plot was verified by measuring the chamber readings at 50 V, 100 V, 150 V, 200 V, 250 V, 300 V, 350 V and 400 V.

To determine the output factors from detector readings, the measurements were conducted by maintaining the detector at a fixed position while altering the field size. To investigate the difference in output influenced by magnetic field, measurements for square isocentric fields were performed at maximum position of each field and at CAX position.

For isocentric fields, the detector was positioned at the CAX, and the field size was adjusted from a small size to the f_{msr} size. In the case of off-axis fields, the detector was shifted from isocenter while remaining at the CAX of the field. The ratio of detector readings for off-axis fields refers to the f_{msr} that were shifted by the same distance and in the same direction as the small field.

2.4 Monte Carlo simulations

The Monte Carlo (MC) method is a computational technique that provides a numerical solution to problems by randomly sampling on known probability distributions. In the field of radiation therapy, radiation transport MC simulations (hereafter referred to simply as MC) have been employed since the late 1970s and have become an essential tool for dose calculations and treatment planning. MC simulations in radiation therapy are commonly used for estimation of stopping-power ratios, perturbation factors for ionization chambers and correction factors related to beam quality and small field dosimetry [77] [78].

In radiation therapy, MC simulates the radiation transport of many single particles by tracking their trajectory through interactions in material of a well-defined simulation geometry. Interaction of the particles are determined using known atomic cross-sections that determine the probability of the interactions. Random numbers are sampled to determine if and which interaction occurs, to determine the energy loss, the direction of particle scattering as well as to

generate new particles. In radiation therapy, the focus is typically on the local energy deposition to determine the absorbed dose distribution. While the dose distribution resulting from a few particle tracks have a large statistical uncertainty, repeating the simulation millions of times leads to uncertainties in the order of only 0.1 %. This iterative approach allows for obtaining a mean value and a standard deviation of required quantity [61].

The development of IgRT has further emphasized the need for MC simulations. These simulations allow for the optimization of treatment plans based on the four-dimensional imaging data. Moreover, MC simulations play a key role in ensuring accurate dosimetry verification, enhancing the precision and safety of IgRT [79]. MC simulations allow to study setups that can not be readily implemented experimentally and decouple the problem into different components. In MRgRT, certain dose measurements in the presence of magnetic fields still pose challenges. MC simulation offer the advantage of easily altering the direction and intensity of the magnetic field, thereby providing valuable insights for dosimetry in magnetic fields. However, accurate particle transport is crucial for reliable dose calculations. The accuracy of transport algorithms is typically assessed using the Fano cavity test, which aims to determine if the simulation accurately reproduces the expected behavior according to the Fano theorem [80]. Nevertheless, special conditions need to be defined when performing the Fano test in magnetic fields [81].

MC toolkits (i.e. a collection of tools) are software packages that use the MC method for a specific purpose. In this thesis, two MC toolkits were used: For simulation of photon irradiations in magnetic fields, EGSnrc (Electron Gamma Shower) [82] [83], while for carbon-ions, TOPAS (TOol for PArticle Simulation) [84] [85] based on Geant4 [86] was employed. Both toolkits are C++ written packages designed for particle transport simulations. EGSnrc is considered to be the gold standard for photon and electron transport. However, it lacks the ability to simulate heavy charged particles, such as protons and heavier ions. TOPAS, on the other hand is able to simulate a broader set of ionizing particles [85], including ions, although it is less computationally efficient than EGSnrc when it comes to simulating electron transport [87]. Specifically, the EGSnrc version released in 2020 [82] was used with enhanced EEMF (Electron-Electron Magnetic Field) subroutines [88], for the transport of charged particles in the presence of electromagnetic field. Also, used TOPAS version 3.7 is able to simulate the radiation transport in magnetic fields.

2.4.1 Simulations of carbon-ion reference dosimetry in magnetic fields

2.4.1.1 Particle transport

The particle transport is performed in discrete steps and consists of the free path length between two interactions, the type of interaction and the scattering angle. These steps are repeated until either all particles have exited the defined simulation geometry or until their energy drops below a specified cut-off energy. When the energy of the particle drops below the cut-off energy, it is assumed that the particle stops and deposits its remaining energy locally in the surrounding medium [77]. In this work, a cut-off value of 0.001 mm was chosen for the residual range of the electrons using the parameter *CutForElectron*.

The *transport parameters* determine how the particles propagate through the simulated geometry. By adjusting these parameters, the user can optimize the simulation to achieve a balance between accuracy and computational time. To control the maximum length of a step in relation to the residual range of the particle [89] the parameter *DRoverR* was set to 0.001. As a particle loses energy, the maximum length of a step decreases until it drops below *finalRange*, below which its transport is terminated in a single step. The *finalRange* parameter was set to 0.01 mm.

To describe various the different interaction processes of particle with matter, TOPAS provides so-called *physics lists*. The choice and configuration of the physics list depend on the specific application and required accuracy for scored quantity. For this project, the default TOPAS physics list was applied, which contained *g4em-standard_opt4* for electromagnetic physics, *g4decay* for decay of secondary particles, *g4h-elastic_HP* and *g4h-phy_QGSP_BIC_HP* for hadronic physics, *g4stopping* for energy loss calculations, *g4ion-binarycascade* for the inelastic ion interactions.

For the transport parameters used in this work, the Fano cavity test was performed in TOPAS within another PhD-thesis (for details, see [90]). Specifically, the test was performed for protons and electrons under magnetic flux densities of up to 1.5 T. The results indicate that the TOPAS passed the Fano test within an uncertainty of better than 0.82 % for protons and 0.39 % for electrons, respectively [90]. Based on these results, and assuming similar results for of carbon-ions, the electron and proton transport parameters as well as the transport parameters in presence of a magnetic field were used in this present work.

2.4.1.2 Chamber response in magnetic fields

The effect of the magnetic fields on the chamber response was described using the $k_{\vec{B},M,Q}$ factor (see equation (2.22)), in the same way as in the experimental measurements. The geometry of the simulations was implemented to closely mimic the experimental setup (described in section 2.3.1) while also aiming to reduce computational time.

The initial geometry of the six chambers (R1-R6) was created in EGSnrc by Spindeldreier et al. [44] and later converted to TOPAS using Geant4 solid shapes. Additionally, the chamber design blueprints (PTW, Freiburg, Germany) were utilized, along with a μ CT scans of the chambers (refer to Figure 2.10), for further fine-tuning of the chamber models.

In order to calculate the $k_{\vec{B},M,Q}$ factor, the energy deposition was scored in the effective sensitive volume of the chamber. It has been observed in previous studies with photons that the presence of dead volume significantly affects the chamber response in magnetic fields [44] [91]. These studies have shown that excluding the dead volume from the sensitive volume in MC simulations improves the agreement with experimental measurements. Consequently, in the present simulations, the effective sensitive volume was defined as sensitive volume from which the dead volume was excluded. The dead volumes were modeled as cylindrical-shaped air slabs adjacent to the chamber stem, with thicknesses of 0.08 cm, 0.09 cm, 0.11 cm, 0.19 cm, 0.22 cm, and 0.26 cm for chambers R1 to R6, respectively. The modelling of the dead volume was adopted from Spindeldreier et al. [44].

As in the experiment, the implemented ionization chamber model was positioned at 2 cm depth in water of volume $12 \times 3.5 \times 10 \text{ cm}^3$ representing the water phantom. The beam was simulated as $(3 \times 6) \text{ cm}^2$ field size, with *Genericlon (6,12)* used as the source for carbon-ions and energy of 390.75 MeV/u. To reduce computation time, the beam size was reduced from 10 cm to 6 cm in the vertical direction while ensuring that the chamber remained fully covered by the beam.

As in the experiment, a uniform magnetic field was delivered to the water phantom, with the orientation perpendicular to both the carbon-ion beam and the ionization chamber direction.

2.4.1.3 Local dose change in magnetic fields

The local dose change in the presence of magnetic fields was quantified using the $c_{\vec{B}}$ factor, as described in equation (2.21). To calculate the $c_{\vec{B}}$ factor, the dose with and without magnetic fields was calculated in 1 cm³ water voxel with a resolution of 1 mm³. The water voxel located within a larger water phantom of 1m³ at a depth of 2 cm, and the similar beam characteristics were employed as in the calculation of the $k_{\vec{B},M,Q}$ factor (see previous section). The ratio of doses with and without magnetic fields was computed to obtain the $c_{\vec{B}}$ factor for different magnetic flux densities ranging from 0.1 to 1 Tesla.

2.4.2 Simulations of small photon field dosimetry in magnetic fields

The small field photon dosimetry measurements in magnetic fields were performed as part of the EMPIR (European Metrology Programme for Innovation and Research) funded project “Traceable Dosimetry for Small fields in MR-guided RadioTherapy (MRgRT-DOS)” Within this project, MC calculations for the ViewRay MRidian MR-Linac have been performed by consortium partners from the NPL using EGSnrc. As the information on the phase space required for the MC simulation could not be obtained from the vendor of the MR-Linac, the partners from NPL developed their own beam model. To adjust and validate the beam model, the results of the scanning measurements described in the previous section were provided. After successful validation, full source phase space data was generated and based on the obtained phase space data, the small photon field dosimetry measurements performed in this thesis were simulated by the partners from NPL using the EGSnrc MC code.

The self-consistency test of the EGSnrc MC code successfully passed the Fano test on small cavities, validating the employed transport parameters. Simulations were performed using the C++ user codes *cavity* and *egs_chamber*, designed for or calculating the response of ionization chambers. It was assumed that the simulated reading of the ionization chamber is proportional to the dose to the sensitive volume, and this proportionality factor was assumed to be independent of field size and beam quality. The simulation geometry was designed to mimic the experimental measurements described in section 0, with a constant and uniform magnetic field. The design of the PTW PinPoint 3D and the PTW microDiamond detectors was modelled according to the detector design blueprints (PTW, Freiburg, Germany). The dead volume of the PinPoint 3D detector was simulated as a series of stacked cones above the guard electrode, which was obtained from finite element modeling using the COMSOL package. The chamber geometry was updated to exclude these volumes in the calculation of chamber response. Results of these simulations at NPL were provided for comparison with the measurements performed within this thesis.

3 Results

3.1 Carbon-ion reference dosimetry in magnetic fields

3.1.1 Polarity and ion recombination corrections

The polarity correction factors k_{pol} for the commercially available R3 chamber were found to be unity for all tested magnetic flux densities, with an uncertainty of less than 0.25 % over three measurements. This data is summarized in Table 3.1.

Table 3.1 Polarity k_{pol} and ion recombination k_s correction factors with standard deviations for the R3 chamber (PTW 30013) irradiated with 390.75 MeV/u carbon-ion beam in presence of representative magnetic flux densities.

$B [T]$	k_{pol}	k_s
0.0	0.9998 ± 0.0025	1.0062 ± 0.0021
0.2	0.9998 ± 0.0020	1.0063 ± 0.0014
0.3	1.0001 ± 0.0014	1.0062 ± 0.0009
1.0	0.9998 ± 0.0009	1.0062 ± 0.0020

The Jaffé-plots for the R3 chamber show linear behaviour between $1/M$ and $1/V$ for voltages ranging from 50 V to 400 V, over all tested magnetic flux densities (see Figure 3.1). This linearity validates the use of the two-voltage method to calculate ion recombination correction factors k_s . The calculated values of k_s show variations of only 0.01 % among the tested magnetic flux densities and is within the range of standard deviation for three measurements taken at each magnetic flux density. The calculated k_s values for voltages of 400 V and 50 V are also presented in Table 3.1.

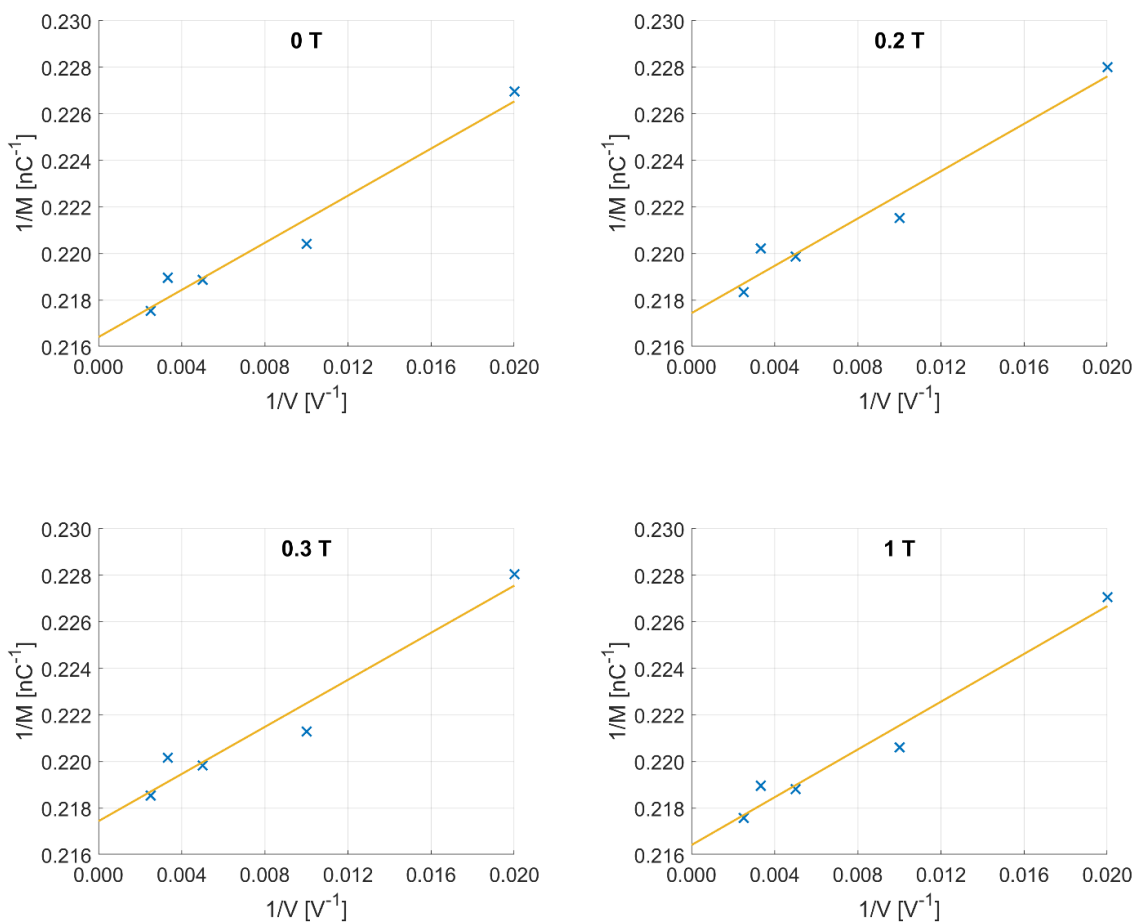


Figure 3.1 Jaffé-plots for the R3 chamber (PTW 30013) irradiated with 390.75 MeV/u carbon-ion beam at 0, 0.1, 0.2 and 1 T. The solid lines illustrate the linear fit to the data.

3.1.2 Chamber response in magnetic fields

The response of the six Farmer-type chambers in the presence of magnetic fields was first investigated for carbon-ion with beam energy of 390 MeV/u. All six chambers exhibited a change in the response depending on the magnetic flux density. Figure 3.2 shows the variation of experimentally measured and Monte Carlo simulated $k_{\vec{B},M,Q}$ values with different magnetic flux densities. Small perturbations of $k_{\vec{B},M,Q}$ with different magnetic flux densities are observed. The dependence is non-linear for all six chambers and is also influenced by the chamber volume.

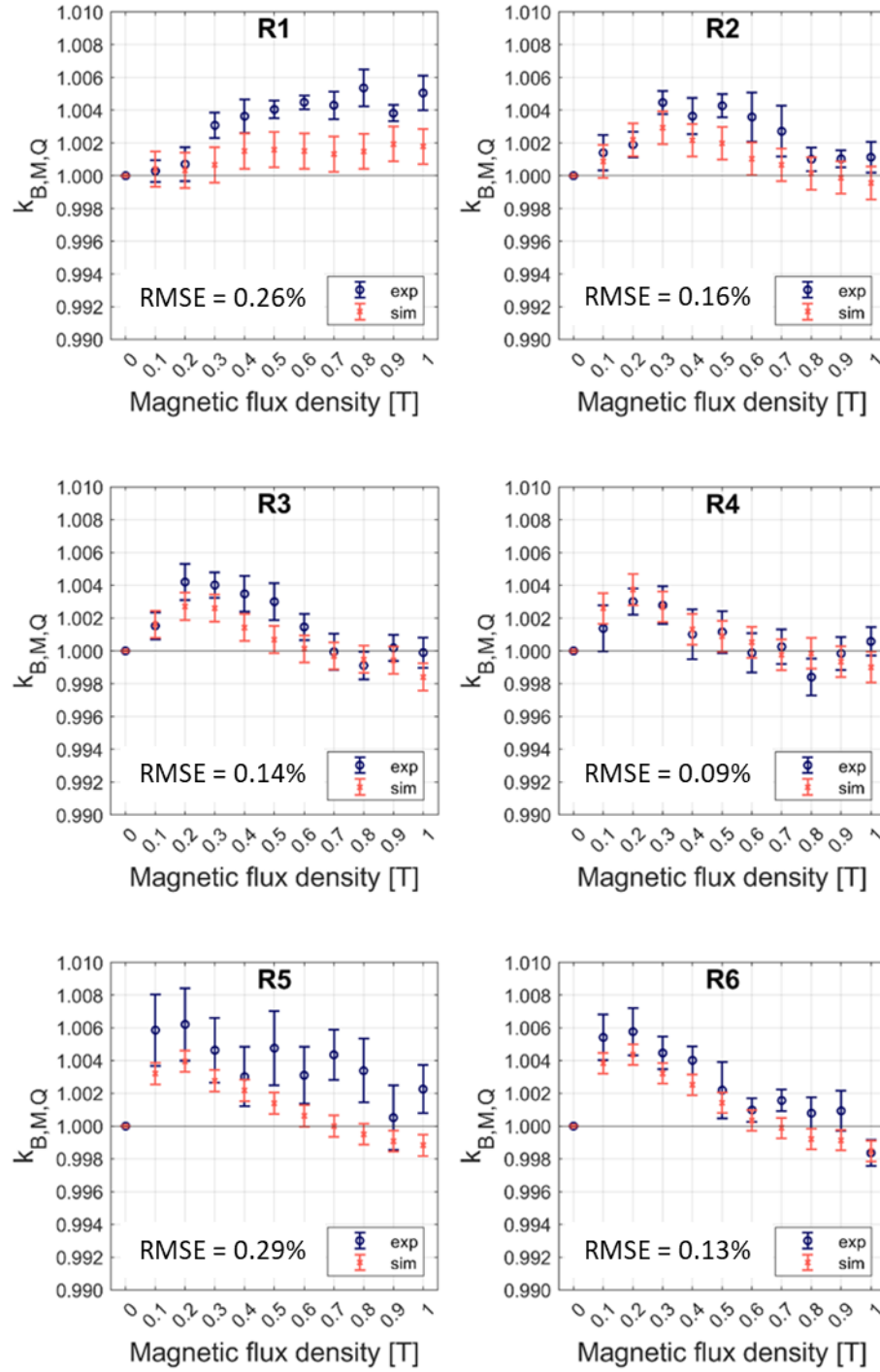


Figure 3.2 Impact of the magnetic field on the response of six Farmer-type chambers irradiated with 390.75 MeV/u carbon-ion beam: experimentally measured (blue points) and simulated (red points) $k_{B,M,Q}$ values as function of the magnetic flux density. The error bars indicate the standard error of the mean.

The experimental results show the most significant changes in $k_{\vec{B},M,Q}$ values at 0.2 T for chambers R3-R6. Chamber R5 exhibited the greatest change of $(0.62 \pm 0.22) \%$, followed closely by the chamber R6 with a change of $(0.58 \pm 0.14) \%$. For the chambers R3 and R4, the maximum changes were $(0.42 \pm 0.11) \%$ and $(0.30 \pm 0.08) \%$, respectively. Chamber R2 exhibited a maximum change of $(0.45 \pm 0.07) \%$ at a magnetic field strength of 0.3 T, while the smallest chamber, R1, reached its maximum change of $(0.54 \pm 0.11) \%$ at 0.8 T. The detailed results of the measured $k_{\vec{B},M,Q}$ values for all six chambers, along with the p-values from the Shapiro-Wilk test and the Student's t-test, can be found in Appendix

Table A.1 in the appendix.

The simulated $k_{\vec{B},M,Q}$ values across varying magnetic flux densities exhibited a similar trend as the experimental measurements for all six chambers. This trend indicated an increase in $k_{\vec{B},M,Q}$ values as the magnetic flux density increased, followed by a decrease to values close to unity for detectors R2-R6 at high magnetic flux density. However, chamber R1, showed a continuous increase in $k_{\vec{B},M,Q}$ values with increasing magnetic flux density. The maximum increase of $(0.44 \pm 0.06) \%$ and $(0.40 \pm 0.07) \%$ occur at a magnetic field strength of 0.2 T for chambers R6 and R5 respectively. For the chambers R3 and R4, the maximum simulated change is at 0.2 T with an increase of $(0.27 \pm 0.08) \%$ and $(0.37 \pm 0.09) \%$ respectively. Chamber R2 reached the maximum change of the $k_{\vec{B},M,Q}$ value at 0.3 T with $(0.29 \pm 0.09) \%$. The smallest chamber, R1, exhibited a change of $(0.19 \pm 0.09) \%$ at 0.9 T.

The agreement between the simulated and measured results was evaluated using the root mean square error (RMSE). The RMSE values for chambers R3-R6 indicate a very good agreement of 0.1 %. However, for the smaller chambers R2 and R1, the agreement is slightly higher with RMSE values of 0.2 % and 0.3 %, respectively.

The beam energy on the $k_{\vec{B},M,Q}$ factor was investigated for the chamber R3 using 200.28 MeV/u and 390.75 MeV/u. As shown in Figure 3.3, the effect of the magnetic field on the response of the R3 chamber was studied. The $k_{\vec{B},M,Q}$ factors for two energies showed similar trend with differences of less than 0.2 % at all magnetic flux densities. However, for all magnetic flux densities, except at 0.1 and 0.8 T, the values of $k_{\vec{B},M,Q}$ at lower energy were consistently lower compared to the values at higher energy.

3.1.3 Local dose change in magnetic fields

The Monte Carlo simulated local dose change $c_{\vec{B}}$ at the measurement position as a function of magnetic flux density is presented in Figure 3.4. The maximum variation of $c_{\vec{B}}$ from unity was found to be $(0.03 \pm 0.08) \%$ for the carbon-ion beam energy of 390.75 MeV/u.

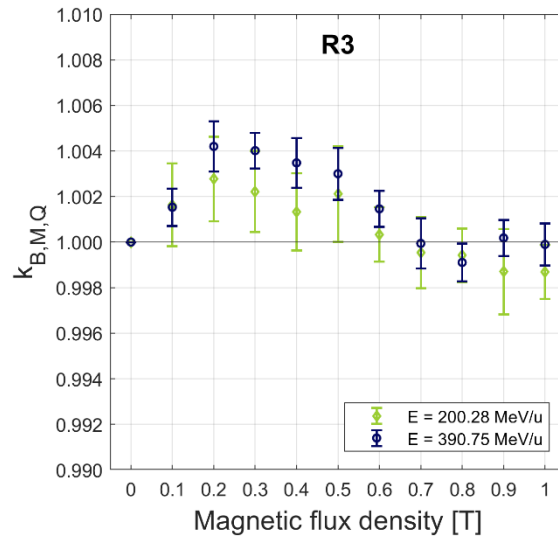


Figure 3.3 Impact of the magnetic field on the response of R3 chamber irradiated with carbon-ion beam energies of 200.28 MeV/u (green points) and 390.75 MeV/u (blue points): experimentally measured $k_{\vec{B},M,Q}$ values as function of the magnetic flux density. The error bars indicate the standard error of the mean.

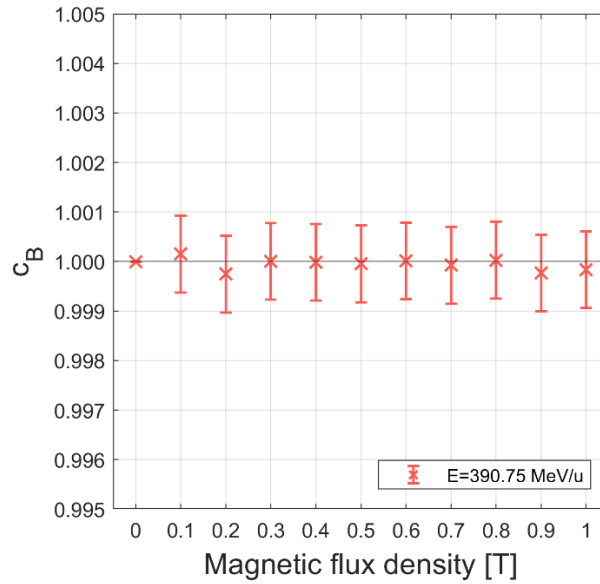


Figure 3.4 Simulated $c_{\vec{B}}$ values for different magnetic flux densities, for carbon-ion beam of 390.75 MeV/u. The error bars indicate the standard deviation.

3.1.4 Magnetic field correction factors

The magnetic field correction factor $k_{\vec{B},Q}$ was calculated as the product of the measured $k_{\vec{B},M,Q}$ factors and simulated $c_{\vec{B}}$ factors.

Table 3.2 lists the $k_{\vec{B},Q}$ values for the commercially available R3 chamber at different magnetic flux densities for carbon-ion beam of 390.75 MeV/u. The maximum deviation of $k_{\vec{B},Q}$ from unity for R3 chamber was observed at 0.3 T, with an increase of (0.40 ± 0.11) %.

Table 3.2 The magnetic field correction factor $k_{\vec{B},Q}$ for the R3 (PTW 30013) chamber obtained by multiplying the measured $k_{\vec{B},M,Q}$ factor and the simulated $c_{\vec{B}}$ factor.

B [T]	$k_{\vec{B},M,Q}$	$\sigma(k_{\vec{B},M,Q})$	$c_{\vec{B}}$	$\sigma(c_{\vec{B}})$	$k_{\vec{B},Q}$	$\sigma(k_{\vec{B},Q})$
0.0	1.0000	-	1.0000	-	1.0000	-
0.1	1.0015	0.0008	1.0002	0.0008	1.0017	0.0011
0.2	1.0042	0.0011	0.9997	0.0008	1.0039	0.0013
0.3	1.0040	0.0008	1.0000	0.0008	1.0040	0.0011
0.4	1.0035	0.0011	1.0000	0.0008	1.0035	0.0013
0.5	1.0030	0.0011	1.0000	0.0008	1.0030	0.0014
0.6	1.0015	0.0008	1.0000	0.0008	1.0015	0.0011
0.7	0.9999	0.0011	0.9999	0.0008	0.9999	0.0014
0.8	0.9991	0.0008	1.0000	0.0008	0.9991	0.0011
0.9	1.0002	0.0008	0.9998	0.0008	1.0000	0.0011
1.0	0.9999	0.0009	0.9998	0.0008	0.9997	0.0012

The $k_{\vec{B},Q}$ factors for the remaining five chambers can be found in Table A.2 in the appendix. An overall maximum deviation of 0.6 % from unity is observed across all chambers.

3.2 Small photon field dosimetry in magnetic fields

3.2.1 Reproducibility and additional influence factors

The reproducibility of the experimental setup was quantified by measuring output variations at the 0.35 T MR-Linac for the small fields using the PTW PinPoint 3D (31022) chamber. Repeated measurements of chamber reading for a nominal field size of $(1.66 \times 1.66) \text{ cm}^2$ showed that the output of the MR-Linac varies within 0.65 % uncertainty from day to day, and only less than 0.07 % within the measurement session. Therefore, further measurements of the small and reference fields were conducted on the same day to ensure consistent output factor calculations.

Measurements of the PinPoint 3D chamber reading for small square isocentric fields were measured at both, the CAX and the maximum position of each field. The results listed in Table 3.3 indicate that the difference in the chamber reading between these two positions are within the range of the standard deviation and thus negligible. Consequently, it was determined that positioning the detector at the CAX for isocentric fields during output factor measurements is appropriate and ensures consistent and reliable measurements.

Table 3.3 The differences in PinPoint 3D chamber reading at at the CAX and the maximum position of the presented isocentric small fields, along with the corresponding standard deviations.

Nominal Field Size [cm^2]	Δ (MAX, CAX) [%]
3.32 x 3.32	0.20 ± 0.22
2.48 x 2.49	0.13 ± 0.19
1.66 x 1.66	0.08 ± 0.15
0.82 x 0.83	0.07 ± 0.10

The investigation of polarity and ion recombination correction factors was performed for the PinPoint 3D chamber, considering both machine-specific reference f_{msr} and small field sizes. Measurements at opposing polarizing potentials led to the polarity correction factor k_{pol} , which are also presented in Table 3.4. The linearity of the Jaffé-plots presented in Figure 3.5 allowed the use of the two-voltage method to calculate ion recombination correction factors k_s presented in Table 3.4. These results showed that k_{pol} and k_s were independent of the field size.

Table 3.4 Polarity k_{pol} and ion recombination k_s correction factors with standard deviations for the PinPoint 3D chamber for a machine-specific reference field and a small field.

Nominal Field Size [cm ²]	k_{pol}	k_s
9.96 x 9.96	0.9988 ± 0.0006	1.0049 ± 0.0005
1.66 x 1.66	0.9990 ± 0.0005	1.0046 ± 0.0008

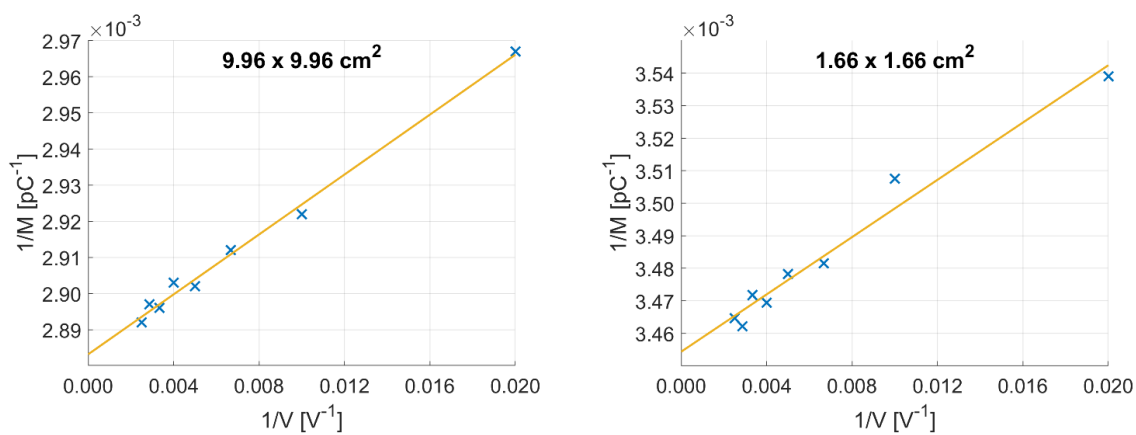


Figure 3.5 Jaffé-plots for machine-specific reference and a small isocentric field. The crosses in the figure represent the measured data obtained using the PinPoint 3D chamber, while the solid line represents the linear fit to the data.

3.2.2 Dose distribution

The dose distribution of the MR-Linac in the 0.35 T magnetic field was studied using two types of dose profiles. These profiles were obtained with the motorized water phantom, as described in section 2.3.2.2. The first type of profile examined was the percentage depth dose (PDD). Figure 3.6. presents the PDD profiles for square isocentric small fields and machine-specific reference field.

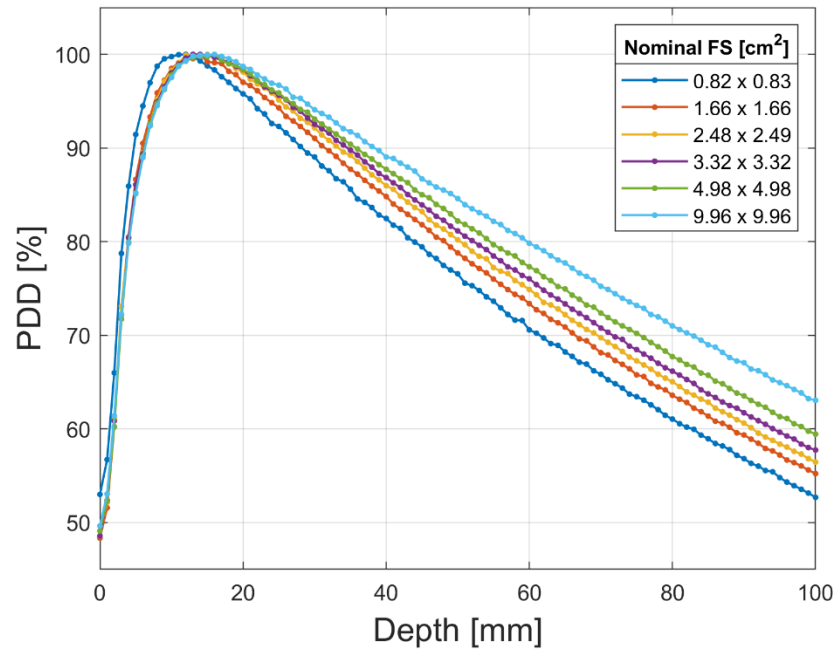


Figure 3.6 Percentage depth dose curve for isocentric square fields of different nominal field sizes including the machine-specific reference field measured with PinPoint 3D chamber.

Lateral profiles were performed to find the dosimetric field size defined as FWHM at the point of output factor measurements (SSD = 85 cm and SAD = 90 cm). The FWHM values of the X and Y profiles measured with the PinPoint 3D and microDiamond detectors were utilized to calculate the equivalent square field size S_{eq} associated with the output factor, using equation (2.29). Lateral profile measurements were performed for square isocentric, rectangular isocentric and square off-axis fields. Examples of these profiles are presented in Figure 3.7, Figure 3.8 and Figure 3.9 respectively.

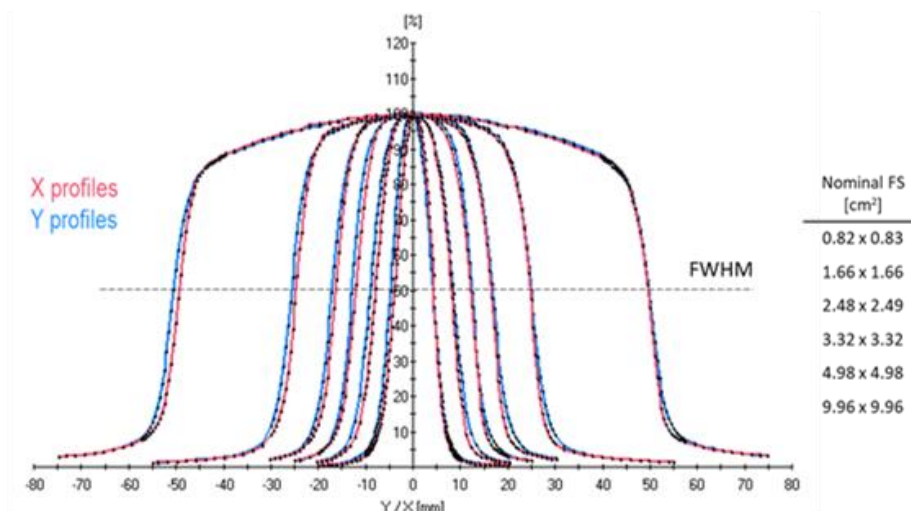


Figure 3.7 Lateral profiles of small isocentric square fields and machine-specific reference field measured with PinPoint 3D chamber. Nominal field sizes are presented in the form of (X x Y) cm².

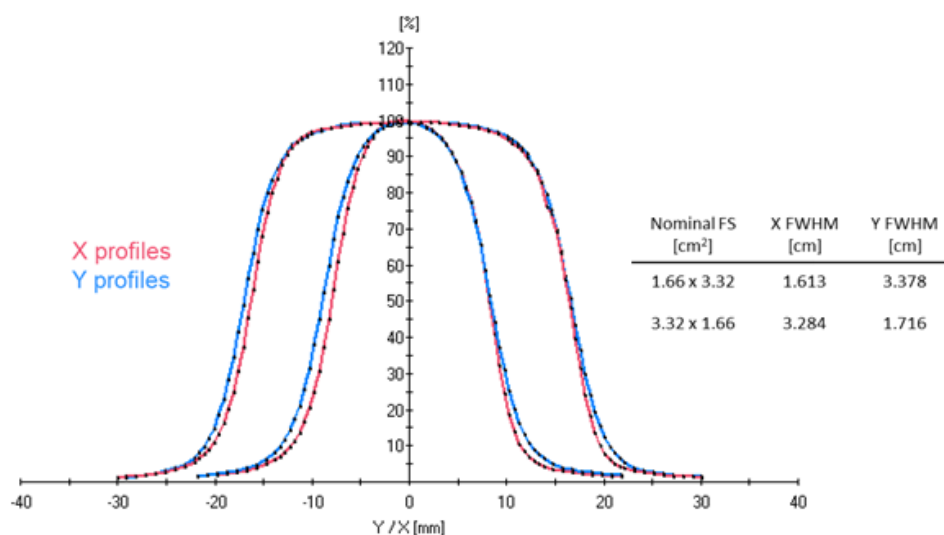


Figure 3.8 Lateral profiles of a (1.66 x 3.32) cm² and (3.32 x 1.66) cm² isocentric rectangular fields measured with PinPoint 3D chamber. Nominal field sizes are presented in the form of (X x Y) cm².

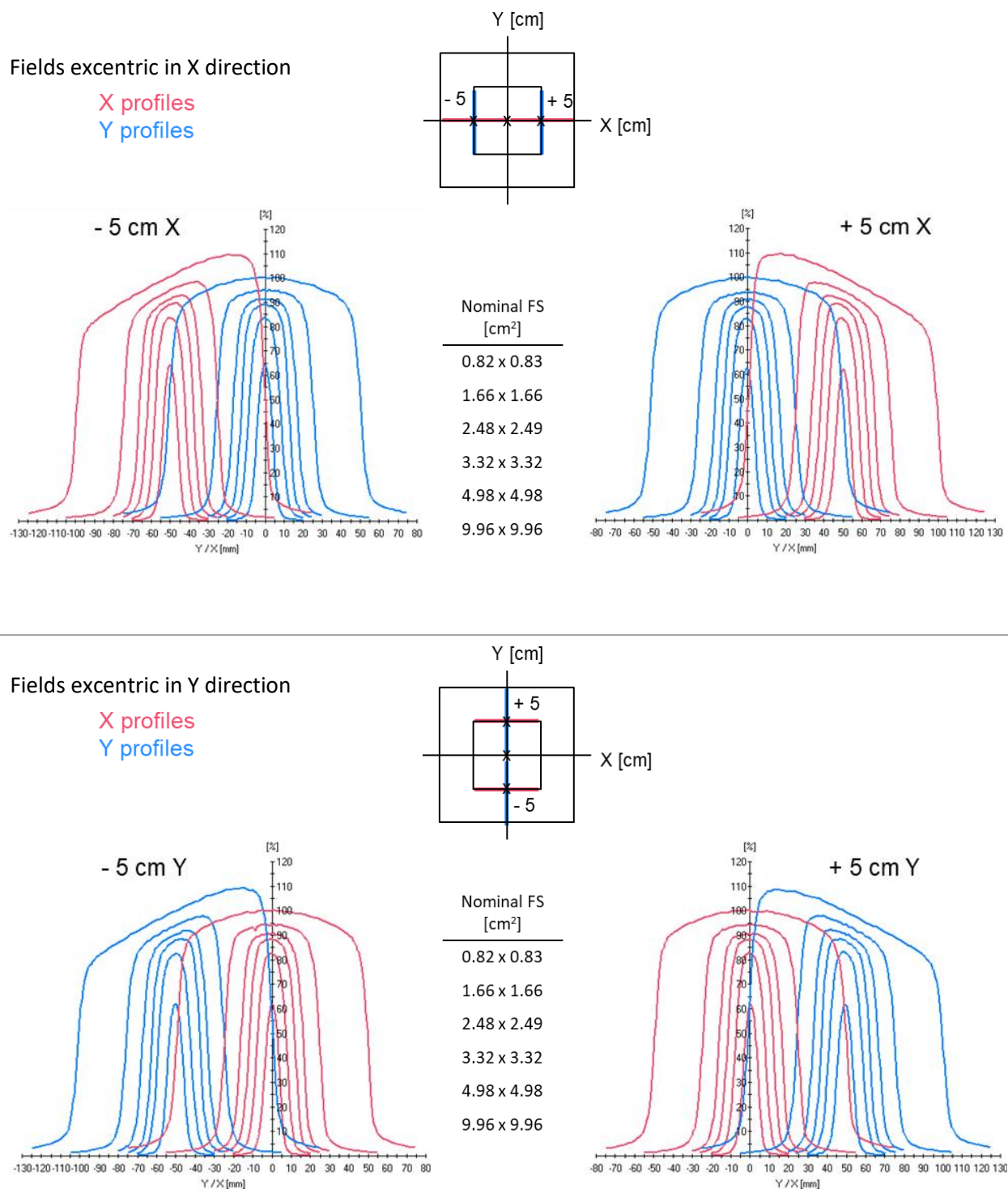


Figure 3.9 Lateral profile measurements with PinPoint 3D chamber for square off-axis fields shifted 5 cm from the machine isocenter in X and Y directions, respectively. Nominal field sizes are presented in the form of (X x Y) cm².

The calculated values of S_{eq} for isocentric square and isocentric rectangular fields are presented in Table 3.5 and Table 3.6 respectively. For square off-axis fields, S_{eq} deviated from the respective S_{eq} of isocentric square fields by less than 1.5 % for the PinPoint 3D chamber and less than 1 % for the microDiamond detector.

For simplicity, field sizes in this section are referred to by their nominal values (collimator openings indicated as (X x Y) cm²) rather than their exact dosimetric S_{eq} values. Also, to maintain brevity, the S_{eq} are denoted by their side length. For example, instead of using the notation (1.66 x 1.66) cm², 1.66 cm is used.

Table 3.5 Measured equivalent square field sizes S_{eq} over three days for square isocentric fields with standard deviations using PinPoint 3D and microDiamond detector.

Nominal Field Size		$S_{eq} = 2XY/(X + Y)$ [cm]	
X [cm]	Y [cm]	PinPoint 3D	microDiamond
9.96	9.96	10.027 ± 0.014	10.046 ± 0.002
4.98	4.98	5.031 ± 0.018	5.033 ± 0.009
3.32	3.32	3.351 ± 0.023	3.354 ± 0.007
2.49	2.48	2.498 ± 0.027	2.494 ± 0.003
1.66	1.66	1.678 ± 0.015	1.687 ± 0.001
0.83	0.82	0.841 ± 0.018	0.835 ± 0.004

Table 3.6 Measured equivalent square field sizes S_{eq} for rectangular isocentric fields using PinPoint 3D and microDiamond detector.

Nominal Field Size		$S_{eq} = 2XY/(X + Y)$ [cm]	
X [cm]	Y [cm]	PinPoint 3D	microDiamond
3.32	9.96	4.954	5.001
9.96	3.32	5.045	5.056
9.96	1.66	2.923	2.946
1.66	9.96	2.785	2.836
3.32	1.66	2.254	2.272
1.66	3.32	2.183	2.208

3.2.3 Output factors

The ratio of uncorrected detector readings $\frac{M_{B,Q_{clin}}^{f_{clin}}}{M_{B,Q_{msr}}^{f_{msr}}}$ (output factor) measurements were performed for square isocentric, rectangular isocentric and square off-axis fields. The resulting output factor curves were plotted as a function of the corresponding S_{eq} values obtained in the previous section.

The output factor measurements using the PinPoint 3D chamber showed a high reproducibility over three measurement days with a standard deviation of up to only 0.1 % for all the fields, except the smallest one where the deviation was 0.3 % (see Figure 3.10). The output factors measured with the microDiamond detector over three days exhibited low standard deviation of less than 0.1 % across all field sizes.

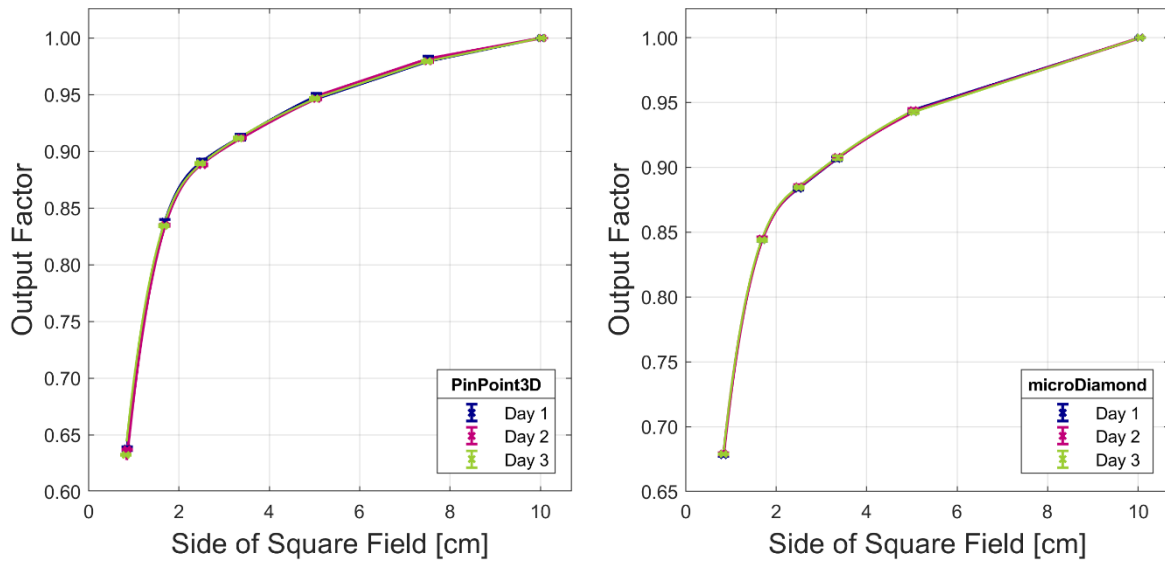


Figure 3.10 Comparison of output factor curves for square isocentric fields measured at three different days with PinPoint 3D chamber (left) and microDiamond detector (right).

The mean output factor values of three-day measurements with PinPoint 3D was compared with the mean output factors measured with the microDiamond detector. The output factors measured with microDiamond exhibited a deviation of less than 1% from those measured with PinPoint 3D, except for the smallest field size, where this deviation exceeded 6%. Both sets of measurements were also compared with the output factors calculated by Monte Carlo simulations. The results are presented in Figure 3.11. On the left side of the figure output factors are normalized to the machine-specific reference field f_{msr} , ($9.96 \times 9.96 \text{ cm}^2$). Since the Monte Carlo values at smaller field sizes were consistently shifted to lower values, the curves were

additionally normalized to an intermediate field f_{int} size of (3.32×3.32) cm², as shown on the right side. This normalization led to a better agreement between measured and simulated data with larger deviations only at (10×10) cm² and at the smallest field size (see discussion in section 4.2.3).

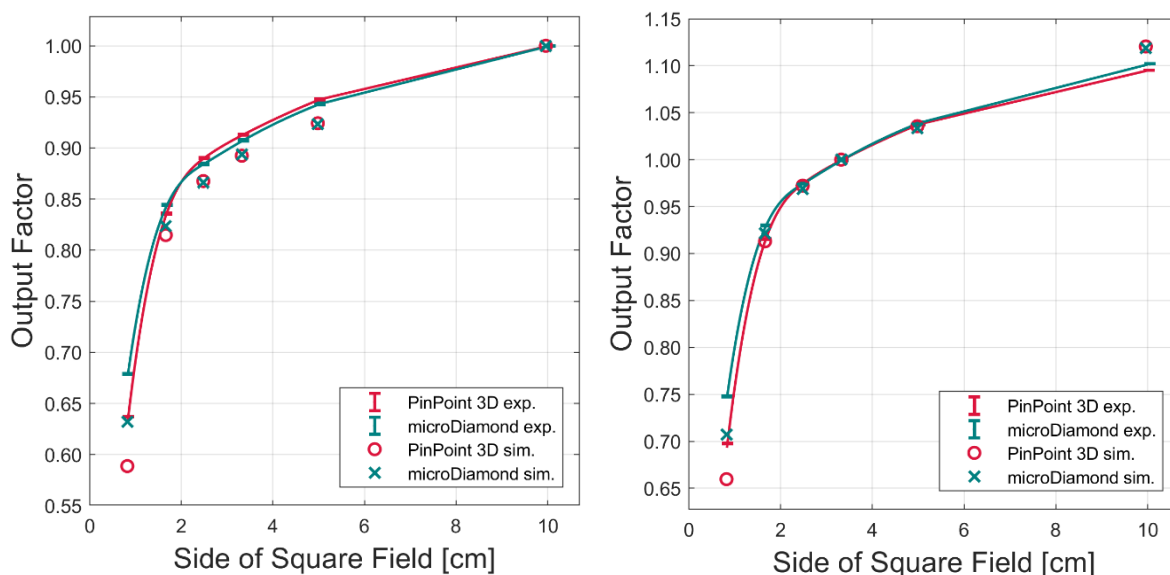


Figure 3.11 Measurements and simulations of output factors for square isocentric fields for PinPoint 3D and microDiamond detectors normalized to the machine-specific reference field (left) and to the intermediate field size (right).

Figure 3.12 shows the comparison of output factors for rectangular fields with the output factor curve obtained for square isocentric fields. To calculate S_{eq} for rectangular fields, two different formulas were utilized – equation (2.28) for the small fields and equation (2.29) for the broad fields. On the left side of Figure 3.12, the S_{eq} values calculated using the formula for small fields are presented. Rectangular fields that fulfil the condition $0.7 < X/Y < 1.4$ for the use of this formula are represented by crosses, while circles indicate rectangular fields that do not meet this condition. On the right side of Figure 3.12, all the rectangular fields were compared using the S_{eq} formula for broad fields, showing an overall better agreement with output factor curve for square fields.

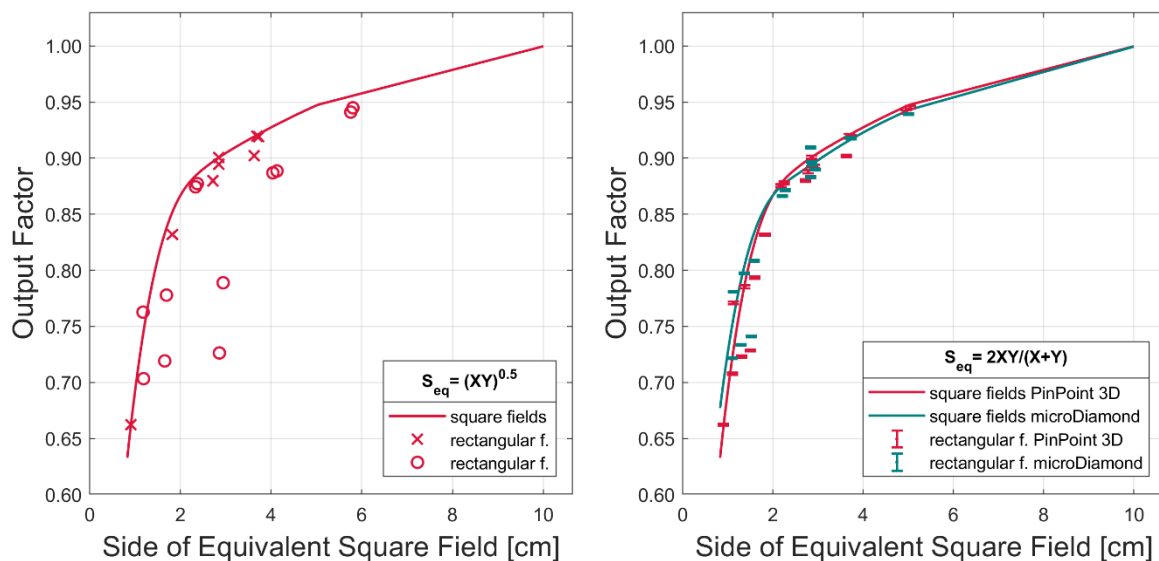


Figure 3.12 Output factors for small rectangular isocentric fields displayed together with the output factor curve for square isocentric fields measured with PinPoint 3D (red) and microDiamond (green) detectors. Equivalent square fields size was calculated with the equation for the small fields (left) and with the equation for the broad fields (right). In the left graph, crosses represent the fields that fulfil the condition of the equation for the small fields, while circles represent fields that do not fulfil this condition.

Figure 3.13 compares four output factor curves for square off-axis fields, measured at four different positions shifted 5 cm from the isocenter, with the output factor curve for square isocentric fields. The measurements were performed using the PinPoint 3D detector on the left and the microDiamond detector on the right. All measurements show a good agreement with their respective isocentric output factors.

For the PinPoint 3D detector, the output factors agree within a deviation of 0.4 % for all the measured fields, except for the smallest field where the deviation is below 1.8 %. For the microDiamond detector, the deviation was below 0.3 % for all the fields, except for the smallest one where the deviation was below 1.5 %.

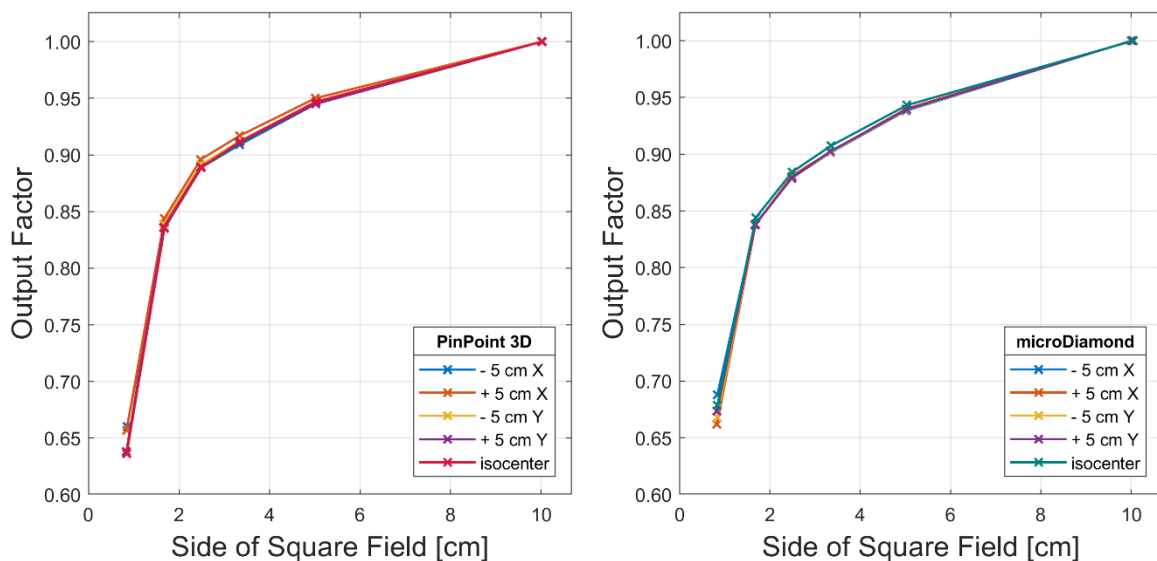


Figure 3.13 Output factor curves for square off-axis fields with the beam axis shifted by 5 cm from the machine isocenter compared with the curve for square isocentric fields. The measurements were performed using the PinPoint 3D chamber (left) and the microDiamond detector (right).

Figure 3.14 provides a comparison of output factor curves for square off-axis fields measured at four different positions, each shifted 5 cm from the isocenter. These measurements were conducted using both the PinPoint 3D and microDiamond detectors. Each output factor value is presented as a function of S_{eq} , obtained from profile measurements using the same detector employed for the output factor measurements.

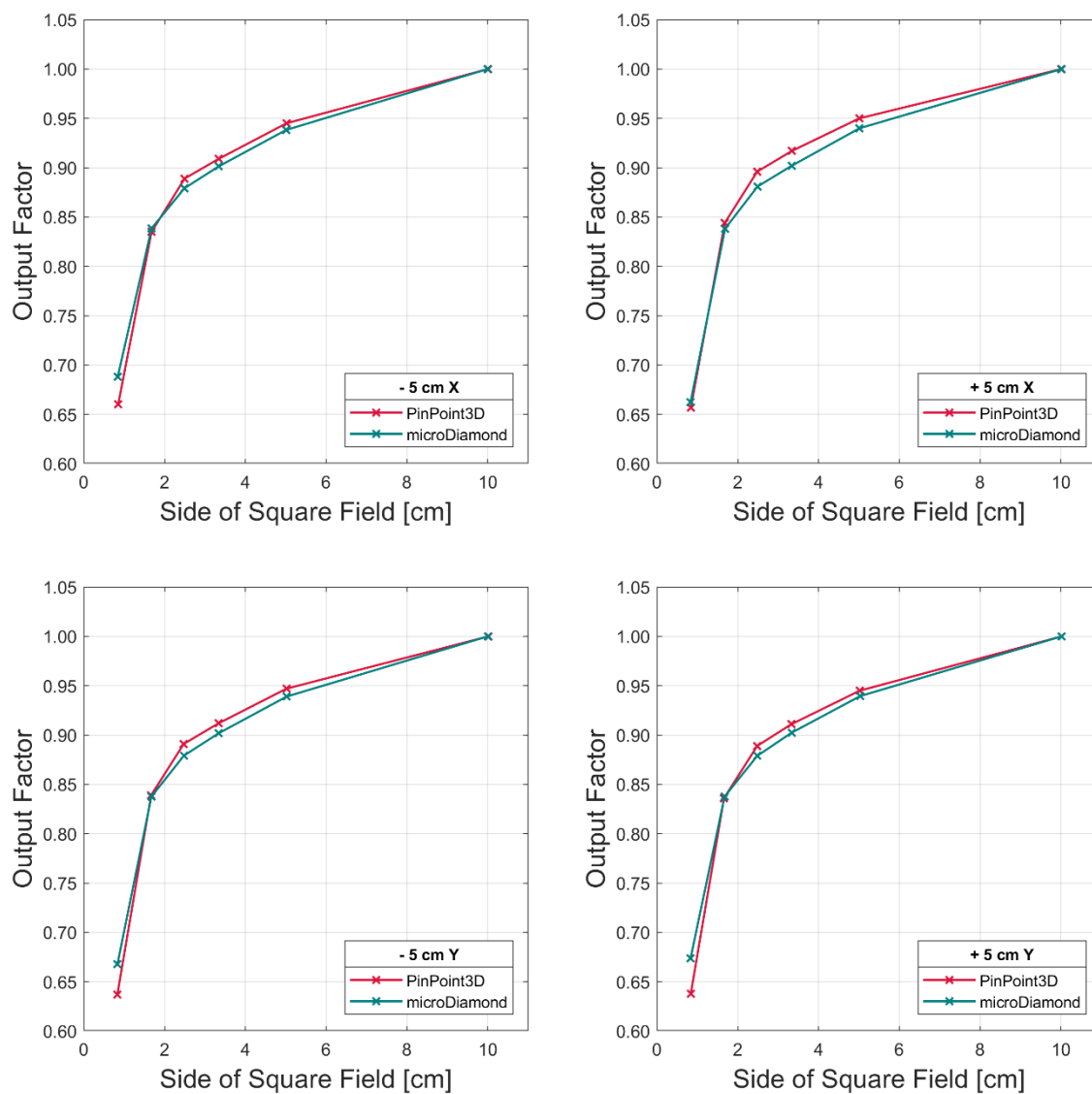


Figure 3.14 Output factor curves for square off-axis fields with the beam axis shifted by 5 cm from the machine isocenter measured with the PinPoint 3D chamber and the microDiamond detector.

3.2.4 Output correction factors

The final output correction factors in the presence of a 0.35 T magnetic field were calculated by dividing the ratio of doses obtained by Monte Carlo simulations by the measured ratio of detector readings (output factors) presented in the previous section, as given in equation (2.34). The simulated results were provided by project partners from NPL, as explained in section 2.4.2.

The detector specific output correction factors for small isocentric square fields are presented in Figure 3.15. Similar to Figure 3.11, where output factors were normalized to f_{msr} as well as f_{int} , the output correction factors are presented as a correction with respect to the machine specific reference and the intermediate field size, i.e. $k_{\vec{B}, Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$ reaches a value of 1 at the field size f_{msr} , while $k_{\vec{B}, Q_{clin}, Q_{int}}^{f_{clin}, f_{int}}$ reaches a value of 1 at the field size f_{int} . As a result of normalization to f_{int} , a better agreement between the corrections calculated solely by Monte Carlo and those determined from the simulated dose ratios and the measured detector reading ratios was obtained, with larger deviations only at (9.96×9.96) cm² and at the smallest field size (see discussion in 4.2.4). The numerical values of these output correction factors for both normalizations can be found in the appendix in Table A.3.

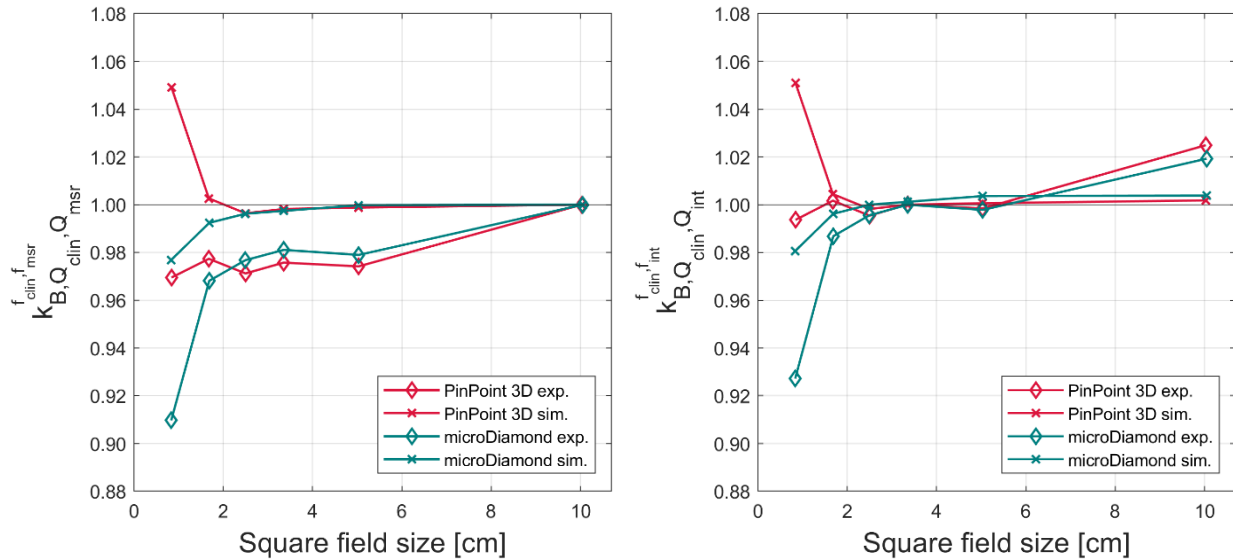


Figure 3.15 Output correction factors for square isocentric fields for the PinPoint 3D and microDiamond detectors normalized to the machine-specific reference field (left) and to an intermediate field size of (3.32×3.32) cm² (right). Simulated values were obtained solely by Monte Carlo while experimental values were obtained from simulated dose ratios and measured detector reading ratios. Connecting lines are provided for the reader's visual guidance.

4 Discussion

4.1 Carbon-ion reference dosimetry in magnetic fields

Correcting for the influence of magnetic fields is crucial to ensure accurate reference dosimetry measurements with ionization chambers in the presence of magnetic fields. This correction is achieved through the application of the magnetic field correction factor $k_{\vec{B},Q}$, which is used to correct the chamber calibration coefficient for the presence of magnetic fields. To determine the $k_{\vec{B},Q}$ factors, thorough investigations are required to understand and quantify the impact of the magnetic field on both, the chamber reading and the local dose change.

In this study, measurements were conducted to investigate the effect of magnetic fields on the response of the commercial Farmer-type chamber (PTW 30013) under carbon-ion beam reference conditions. Additionally, the effects of polarity and ion recombination corrections in magnetic fields were investigated. To explore the chamber volume dependence on the $k_{\vec{B},Q}$, the response of five additional custom-made Farmer-type chambers with varying radius (R1-R6) in magnetic fields were investigated. The $k_{\vec{B},M,Q}$ factors for these six chambers were determined by experimental measurements and Monte Carlo calculations. Furthermore, the study calculated the local dose change in magnetic fields by the $c_{\vec{B}}$ factor, which together with the $k_{\vec{B},M,Q}$ factor provides the final magnetic field correction factor $k_{\vec{B},Q}$ for each chamber, as shown in equation (2.23).

To ensure stable measurement conditions in this study, measures were taken to minimize the impact of the heating of the magnet on chamber readings. This included minimizing the contact surface between the water phantom and magnet pole shoes and integrating a water circulating system into the phantom. These measures have already shown to be effective in previous studies for photon [44] [92] and proton beams [50]. Additionally, limited radiation times with breaks were implemented to mitigate temperature changes. Remaining temperature changes were monitored over time and the impact on the chamber reading was corrected. No dependence of the temperature correction on magnetic flux density was observed. Additionally, the nominal magnetic flux density was validated through measurements, and hysteresis effects were eliminated by randomly selecting the magnetic flux density settings.

The experimental setup was designed to closely resemble the reference dosimetry conditions described in TRS-398 [41]. The chambers were positioned at 2 cm water-equivalent depth in the plateau of a monoenergetic Bragg peak. The TRS-398 recommends a shift of 0.75 times radius of the cylindrical chamber, however in our study this shift was not applied in order to keep the same position for all the chambers during measurements. Since all of the measurements were relative measurements, it can be assumed that this shift would not introduce significant changes in the results. The chambers were irradiated with a (3×10) cm² carbon-ion field. The narrower lateral field width was necessary to achieve magnetic flux densities of up to 1 T and to prevent primary

ion scattering by the magnet pole shoes. However, it can be assumed that lateral charged particle equilibrium is maintained to a good approximation for both primary and secondary ions, as well as for the short-ranging secondary electrons. Therefore, our results are expected to be valid for true dosimetric reference conditions with carbon-ion beams.

4.1.1 Polarity and ion recombination corrections

In general, magnetic fields could potentially affect polarity and ion recombination corrections. However, our study with the commercially available Farmer-type chamber R3 (PTW 30013) for carbon-ion beam of 390.75 MeV/u revealed that the influence of the tested magnetic flux densities on these corrections is not significant. This finding is consistent with previous research conducted by Marot et al. [50] in proton beams, where a PTW 30013 Farmer-type chamber was tested under magnetic flux densities of 0.2, 0.5, 0.7, and 1 T. Additionally, investigations in photon beams by Smit et al. [93] using a NE2571 Farmer-type chamber in a 1.5 T field, and by Spindeldreier et al. [44] with a PTW 30013 Farmer-type ionization chamber in a 0.5 T field, have also demonstrated negligible magnetic field effects on both polarity and ion recombination corrections.

4.1.2 Chamber response in magnetic fields

Measurements conducted using six chambers of varying radii (R1-R6) within magnetic fields revealed complex behavior of the chamber response, dependent on chamber volume and magnetic flux density. All six chamber responses were affected by the magnetic field, with the magnitude of the effect varying according to the magnetic flux density (presented in Figure 3.2). Chambers R2-R6 demonstrated similar behavior in their $k_{\vec{B},M,Q}$ factors, showing a maximum deviation from unity at lower magnetic flux densities followed by a decrease at higher magnetic flux densities. As the chamber radius increased, the magnetic flux density corresponding to the maximum deviation shifted to lower values. Only the chamber R1 displayed a rising $k_{\vec{B},M,Q}$ factor up to a magnetic flux density of 1 T. Because of the pole shoe distance, the investigation of higher magnetic flux densities was limited in our study, preventing the determination of whether a decrease would follow at higher magnetic flux densities.

The R3 chamber was investigated using two different carbon-ion energies, specifically 200.28 MeV/u and 390.75 MeV/u. The dependence of the $k_{\vec{B},M,Q}$ factor on magnetic flux density was found to be similar for both energies. Although the maximum difference observed was only 0.1 %, it was not considered significant. However, in the region where the deviation from unity was the highest (as shown in Figure 3.3), the values obtained for the lower energy were consistently lower. Additionally, the experimental uncertainty at 200.28 MeV/u was slightly

higher compared to 390.75 MeV/u, which could be attributed to the smaller number of measurements taken at the lower energy ($n=13$ compared to $n=19$). Nevertheless, the effect of the $k_{\vec{B},M,Q}$ factors for lower magnetic flux densities is significant for both energy values.

The maximum measured changes observed in the $k_{\vec{B},M,Q}$ factors across all chambers due to the magnetic field effect were found to be within 0.64 %. Since this effect is relatively small, it was necessary to minimize the experimental uncertainty associated with these values. To achieve this, highly reproducible measurement conditions were ensured, and efforts were made to correct for other influence factors such as temperature and pressure. Moreover, dedicated 3D-printed holders were used to guarantee precise day-to-day repositioning of the chambers in the water phantom. The positioning of the water phantom itself was also highly reproducible and was achieved by locking it between the magnet pole shoes that were aligned with the isocenter using the room lasers.

Monte Carlo simulations of the $k_{\vec{B},M,Q}$ factors for all six chambers using a 390.75 MeV/u carbon-ion beam exhibited a similar trend across the tested magnetic flux densities as the measured data (as shown in Figure 3.2). The good agreement between the simulated and measured results was achieved with a RMSE of 0.1 % for chambers R3-R6. Only, for the smaller chambers R2 and R1, the agreement was lower with RMSE values of 0.2 % and 0.3 %, respectively. It should be noted that the largest disagreement observed for the R1 chamber could potentially be attributed to the bent electrode of the chamber, as visible in the μ CT image shown in Figure 2.10. This could have influenced the measurements and was not considered in the simulations. Furthermore, the simulated $k_{\vec{B},M,Q}$ values were consistently lower than the measured values. This discrepancy could be attributed to the lack of precise knowledge of the dead volume in the simulations, which was taken from a previous photon study where the range of secondary electrons is different. While the dead volume was simulated as a slab near the stem, it is likely that real dead volumes have a more toroidal shape. Furthermore, considering the dead and active volumes as simple geometric structures of 0 % and 100 % charge collection efficiency may be too simplistic as simulations of the electric field within the chamber show gradual changes of the electric field [91]. Finally, even for a geometric dead volume, the relative uncertainties in the definition may be larger for small chamber volumes, which might explain the larger RMSE for R1 and R2. To improve the accuracy of the simulations, the dead volume has to be determined more accurately, e.g. by detailed simulation of the electric field as performed by Poijntinger et al. in their study for photons [91].

A further approximation in the simulation is the modeling of the magnetic field neglecting the fringe field of the electromagnet. Implementing a more realistic magnetic field map model including also the fringe field could in principle be considered. However, it appears unlikely that this will significantly change the response of the chamber to the local radiation field and moreover, it would also significantly increase simulation time, which was the reason why it was not attempted to generate a complete field magnetic map in this study.

The available literature on the ionization chamber response in a magnetic fields for ion beams is still very limited [94]. Specifically, no investigations of chamber response in magnetic fields for carbon-ion beams had been conducted until recently. During the writing phase of this thesis, the paper from Fuchs et. al. [52] on the detector response in magnetic fields for carbon-ion beams was published. This work investigated the influence of magnetic fields on the response of four air-filled ionization chambers for 0, 0.25, 0.5, and 1 T. Results for $k_{\vec{B},M,Q}$ for Farmer-type chamber (PTW 30013) showed similar results as observed in this study. The $k_{\vec{B},M,Q}$ values reached maximum deviation from unity 0.25 T and return close to unity at 1 T for both tested carbon-ion beam energies. For 402.8 MeV/u the deviation was $(0.5 \pm 0.3) \%$ and for 272.5 MeV/u the deviation was $(0.4 \pm 0.3) \%$. The consistent findings between the two independent studies confirm the reliability of both measurements significantly improve the understanding of the influence of magnetic fields on the response of ionization chambers in carbon-ion beams. However, a notable difference between the two studies is that in the current work, the investigation of chamber response was conducted with a higher resolution in magnetic flux densities using increments of only 0.1 T. This provided a more precise determination at which magnetic field the effect becomes significant. Furthermore, our study was the first to compare the measured $k_{\vec{B},M,Q}$ factors with Monte Carlo simulations, providing valuable insights into the agreement between experimental measurements and simulation results for the chamber response under the influence of magnetic fields. By using five additional custom-built chambers of the same design as the PTW 30013 chamber but varying inner radii, our study also gained an insight into the impact of the chamber volume on the $k_{\vec{B},M,Q}$ values.

Apart from carbon-ions, the detector response in a magnetic field has also been investigated for protons. Fuchs et al. [51] investigated the response of a commercially available PTW 30013 Farmer-type R3 chamber in magnetic fields for proton energies of 97.4 MeV and 252.7 MeV and observed a similar trend in the $k_{\vec{B},M,Q}$ factor as observed for carbon-ions, with a rise at low magnetic flux densities followed by a decrease. The maximum increase of $k_{\vec{B},M,Q}$ value for energy of 252.7 MeV reaches $(0.3 \pm 0.1) \%$ at 0.25 T. They also observed that at 1 T, the $k_{\vec{B},M,Q}$ factor decreased below unity to $(0.2 \pm 0.2) \%$. Marot et al. [50] studied the response of R1, R3, and R6 chambers in magnetic fields for a 221.05 MeV proton beam and found that the $k_{\vec{B},M,Q}$ factors for all three chambers followed a similar trend as observed for carbon-ions, but with a slightly smaller effect.

Compared to photons, the effect of magnetic fields on chamber response in ion beam is significantly smaller. In the study conducted by Spindeldreier et al. [44], the response of the same six chambers was investigated under the same range of magnetic flux densities. It was observed that chamber R4 experienced a maximum change of $k_{\vec{B},M,Q}$ value of 8.8 % at 0.9 T. However, this finding is not unexpected as the response alteration originates from the secondary electrons that are influenced by the Lorenz force. These secondary electrons have higher energies, longer ranges, and larger gyromagnetic radii compared to those released by ions. The small differences

observed between carbon-ions and protons, or between different energies of the same ion type, are likely associated with the energy-dependent range of the secondary electrons.

To gain a deeper understanding of the reasons behind the chamber response alteration in magnetic fields, more detailed investigations are necessary. This can be achieved through Monte Carlo-based tracking of the secondary electrons and simulating the electric field configuration. It is likely that the electron return effect (ERE) will play a role in the response alteration. Particularly in the presence of magnetic fields, when charged particles are deflected towards or away from these dead volumes, the influence of dead volumes becomes significant. Therefore, a more detailed investigation of these factors is needed to fully understand the response alteration in ionization chambers under the influence of magnetic fields.

4.1.3 Local dose change in magnetic fields

Based on the results presented in Figure 3.4, it can be observed that the magnetic field has no significant effect on the local dose in carbon-ion beams up to 1 T perpendicular magnetic field. The maximum variation of the $c_{\vec{B}}$ factor was found to be $(0.03 \pm 0.08) \%$ at 0.2 T for carbon-ion beam of 390.75 MeV/u. In the paper from Fuchs et. al. [52], the $c_{\vec{B}}$ factor was calculated for 1 T and different carbon-ion beam energies of 186.1 MeV/u, 272.5 MeV/u and 402.8 MeV/u using Monte Carlo simulations using the Monte Carlo tool GATE [95]. The results indicated that the largest deviation from unity of 0.16 %, was observed for the lowest investigated energy of 186.1 MeV/u. For the energy of 402.8 MeV/u, which is the closest to our energy, the maximum deviation of the $c_{\vec{B}}$ factor was found to be 0.06 % which aligns with our findings.

Investigations in proton beam also show negligible variations. Marot et al. [90] used the TOPAS MC toolkit and found maximum calculated effects of up to $(0.10 \pm 0.06) \%$ at 0.7 T for a 221.05 MeV proton beam and a perpendicular magnetic field direction. Similarly, Fuchs et. al. [52] reported a maximum variation of 0.04 % for a 252.7 MeV proton beam at 1T.

4.1.4 Magnetic field correction factors

As observed in this study, the local dose change $c_{\vec{B}}$ due to the magnetic fields was relatively small compared to the variation of the chamber response $k_{\vec{B},M,Q}$. Since the magnetic field correction factor $k_{\vec{B},Q}$ is determined by the combined effect of $k_{\vec{B},M,Q}$ and $c_{\vec{B}}$, it can be concluded that the final correction factor is strongly dominated by $k_{\vec{B},M,Q}$.

For the commercially available PTW 30013 chamber, the $k_{\vec{B},Q}$ factor was found to be up to 0.4 %. In the literature, the magnetic field effect for proton and carbon-ion beams using the same chamber and orientation reported $k_{\vec{B},Q}$ values of up to 0.5 % [50]–[52], which is significantly

smaller than the effect observed for photons, where the literature reports up to 4.6 % for the PTW 30013 chamber at MR-Linacs with perpendicular 1.5 T magnetic flux density [44]–[48], [96]. The largest response alteration among the investigated chambers was found for the R5 chamber (exhibiting a maximum effect of 0.6 % at 0.1 T) while the R4 chamber showed the smallest effects of up to 0.3 % at 0.3 T.

4.2 Small photon field dosimetry in magnetic fields

To the best of our knowledge, this is the first investigation of the output correction factors for the ViewRay MR-Idian device. The detector-specific output correction factors $k_{\vec{B}, Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$ were established through a combination of measured detector reading ratios and simulated dose ratios following the formulation in equation (2.34). Specifically, these $k_{\vec{B}, Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$ corrections were determined for the PinPoint 3D (PTW 31022) ionization chamber in axial orientation (axis perpendicular to the beam and parallel to the magnetic field), and the microDiamond (PTW 60019) detector in axial orientation (axis parallel to the beam and perpendicular to the magnetic field), see Figure 2.15. The orientation of the detectors with respect to the beam was chosen based on the guidelines outlined in the TRS-483.

4.2.1 Reproducibility and additional influence factors

Dosimetry measurements in the small fields are very challenging and time consuming. This is due to the fact that even minor positional uncertainties can result in notable uncertainties in the measurement results. The alignment based on the room lasers with a typical accuracy of 1 mm, are inadequate for achieving the required precision for small fields [49]. Therefore, after initial alignment with lasers, further refinement was performed based on lateral profile measurements. This procedure was performed using the BEAMSCAN software as explained in section 0. Lateral profiles of a (4.98 x 4.98) cm² isocentric field were measured to adjust the phantom isocenter relative to the beam CAX with an accuracy of < 0.6 mm. Furthermore, measurement of two off-axis profiles determined any rotation in the phantom coordinate system with respect to the beam CAX, with the accuracy of < 0.2°, as specified by the vendor [97]. This procedure assured highly accurate alignment of the axes of the water phantom.

In the presence of a magnetic field perpendicular to the beam direction, small fields can exhibit an asymmetry in the dose profile shape with a tilt in the direction of the Lorentz force. Therefore, lateral profile measurements for various small fields were performed to investigate this effect for 0.35 T magnetic field. The shift between CAX of the small fields determined by the center of 50 % isodoses and the previously established isocenter position according to the CAX of (4.98 x 4.98) cm² field was found to be less than 0.4 mm. Given that this shift is less than the alignment accuracy, no CAX correction was applied for the small fields. Additionally, evaluations of detector readings at the maximum position of small isocentric fields showed no significant difference from measurements taken at the CAX position. This observation is detailed in Table 3.3. Consequently, output factors for all isocentric fields were measured at the CAX position that was determined through the alignment procedure.

The reproducibility of the experimental setup and the alignment procedure was tested by conducting multiple measurements of the PinPoint 3D chamber reading for a small field size. This

involved repeated measurements performed three times within a single session, as well as measurements conducted over three different days. Within the same measurement session, the uncertainty of the mean chamber reading was found to be less than 0.07 %, indicating a high level of consistency. Furthermore, the measurements exhibited good reproducibility across different days, with an uncertainty of 0.65 %, affirming the repeatability of the alignment procedure. However, output factors were always obtained from the readings measured on the same day to ensure the same measurements conditions and were then averaged over the different days.

While determination of the output correction factors relies on relative measurements, it is still important to correct for influence factors on chamber reading. Given the extended duration of measurement sessions, atmospheric conditions can exhibit substantial fluctuations [49] which can impact the chamber reading. To mitigate this, temperature and pressure were monitored throughout the output factor measurements. Additionally, polarity and ion recombination correction factors may depend not only on the field size, but also on magnetic fields. In this study, polarity and ion recombination correction factors were investigated in the presence of 0.35 T magnetic field, for machine-specific reference field and a small field size of $(1.66 \times 1.66) \text{ cm}^2$. Results presented in Table 3.3 showed no significant beam size dependence on both correction factors for PinPoint 3D (PTW 31022) in a radial orientation. For the machine-specific reference field under the influence of the 0.35 T magnetic field, the polarity effect was determined to be 0.9988 ± 0.0006 . This value agrees with the values 0.998 and 0.999 previously reported by Vieilleigne et al. [98] and Khee Looe et al. [99] for a 6 MV photon beam without the presence of a magnetic field.

4.2.2 Dose distribution

The investigation of the dose distribution in the 0.35 T MR-Linac involved the measurement of percentage depth dose (PDD) and lateral dose profiles. These measurements were conducted for isocentric square and rectangular fields, as well as for off-axis square fields. The range of examined nominal field sizes varied from $(9.96 \times 9.96) \text{ cm}^2$ down to $(0.82 \times 0.83) \text{ cm}^2$.

The PDD curves for square isocentric fields of diverse sizes are depicted in Figure 3.6, normalized to their respective maximum values. The trends in the alteration of PDD curves with varying field sizes followed patterns observed in the absence of a magnetic field. Specifically, as field size decreases, the depth at which the dose reaches its maximum value decreases, and the slope of the depth dose curves beyond the maximum becomes more pronounced.

Given the recommendation from TRS-483 [49] to utilize the FWHM of the lateral beam profile at the measurement depth for referencing output correction factors, this study involved measuring lateral profiles at SSD = 85 cm and SAD = 90 cm and combining them with the output factor measurements presented in section 3.2.3.

Volume averaging effects caused by detectors can have an influence on profile measurements [100], therefore small field profiles were measured with two detectors of different types. The equivalent square field sizes S_{eq} calculated from FWHM measured using the microDiamond detector differed from those obtained with the PinPoint 3D detector by less than 0.8 %, indicating a good level of agreement. Additionally, the data presented in

Table 3.5 show that S_{eq} derived from the microDiamond measurements exhibited a smaller deviation in comparison to the measurements obtained from the PinPoint 3D chamber. Consistently, the measured Y (in-plane) profiles appeared wider than the X (cross-plane) profiles, as shown in Figure 3.7 and Figure 3.8. For the machine-specific reference field, this difference was 1.7 % when using PinPoint 3D chamber and 1 % with microDiamond detector. For the smallest field size, this increased up to 11.1 % with the PinPoint 3D detector, while the microDiamond detector indicated a difference of 4.7 % between the two profiles. The more pronounced difference between the two profile dimensions for the PinPoint 3D detector in radial orientation can be attributed to the different extensions of the sensitive volume of this detector for the two scanning directions, resulting in different volume effect (see Figure 2.15). In contrast, symmetrical shape of the sensitive volume of the microDiamond detector in axial orientation reduces this difference, likely to result from the arrangement of the multi-leaf collimators, which are oriented in X-direction.

Due to the bore of the MR-Linac, setup corrections of the patient perpendicular to the bore axis are limited. Therefore, the use of small off-axis fields increased with MRgRT applications. Moreover, off-axis fields are not included in the TRS-483. Therefore, this study investigated multiple small off-axis fields shifted 5 cm from the isocenter in four different directions. The profiles of these off-axis fields, as presented in Figure 3.9, exhibit an asymmetrical shape in FFF beams. This asymmetry is characterized by a shift of the maximum position away from the CAX of the field, towards the isocenter. In general, a good agreement below 1 % was observed for the comparison of FWHM measurements between off-axis square fields and square isocentric fields, for most field sizes and both detectors. The largest deviation in FWHM measurements for off-axis square fields, when compared to the FWHM of square isocentric fields, was 1.5 % for the smallest field size when employing the PinPoint 3D detector. However, this deviation was reduced to 0.8 % when the measurements were conducted with the microDiamond detector.

4.2.3 Output factors

Output factors, representing the uncorrected ratio of detector readings $\frac{M_{\bar{B},Q_{clin}}^{f_{clin}}}{M_{\bar{B},Q_{msr}}^{f_{msr}}}$, have to be corrected with output correction factors to obtain the relevant ratio of doses $\frac{D_{\bar{B},Q_{clin}}^{f_{clin}}}{D_{\bar{B},Q_{msr}}^{f_{msr}}}$ (field output factor). While the ratio of detector readings can easily be determined by the user at any clinical site, this is not the case for the output correction factor. In this study, the output correction factors were therefore determined from the measured ratio of detector readings and the simulated field output factors according to equation (2.34).

Given that the previously investigated differences in detector readings between the maximum and the CAX positions for square isocentric fields were found to be negligible, the output factors for all isocentric fields were measured with the detector positioned at the CAX. For off-axis fields, the dose maximum was close to the field edge rather than at the CAX position, as can be seen from lateral profiles presented in Figure 3.9. In this case, two effects are superimposed: (i) the reduced output due to the small field, and (ii) the asymmetric profile of the FFF beam. To separate these two effects, the output factors were measured at CAX for both, the small and an off-axis reference field (similar as for isocentric fields) and it turned out that the resulting output factor agreed well with those of isocentric squared and rectangular fields. For treatment planning, this assures that the dose output of off-axis fields can be factorized into contributions of the FFF beam and of the small field, with the latter being characterized by isocentric field measurements.

Output factor measurements for square isocentric fields were conducted at least three times per day and were repeated over the three different days, as depicted in Figure 3.10. The results demonstrated good reproducibility, with a standard deviation of 0.1% across the different days, and a maximum deviation of 0.3 % for the smallest field size. Output factors measured with microDiamond detector over three days, had standard deviations of less than 0.1 % across all field sizes.

The average output factor values, derived from measurements, were utilized to compute the output correction factors. A comparison was drawn between the average output factor values obtained using the PinPoint 3D and the microDiamond detector (see Figure 3.11). As the field size decreased, a rapid decrease in the output factor was observed with both detectors. The microDiamond detector exhibited deviations of up to 1% compared to the PinPoint 3D measurements across all field sizes, except for the smallest field size, where the deviation reached 6.5%.

Measured output factors were also compared with MC-derived output factors for both detectors. When the data was normalized to the machine-specific reference field f_{msr} , as recommended by TRS-483 (see Figure 3.11 on the left), MC data showed a systematic under response for small field sizes compared to measured data for both detectors. Deviations between measured and

simulated output factors reached up to 3 % for the small fields and up to 8 % for the smallest field size. This highlights a potential issue with the MC simulations at the f_{msr} field size. Therefore, another method suggested by TRS-483 was implemented for a comparison, which involved normalization to an intermediate field size f_{int} , in our case, a field size of (3.32 x 3.32) cm². This method is normally recommended when a suitable detector for the entire range of field sizes is not available [49]. In this case, it is recommended to use an ionization chamber from f_{msr} down to f_{int} and a small field detector below f_{int} . Normalizing to the field size f_{int} resulted in better agreement between measured and simulated output factors for small field sizes (see Figure 3.11 on the right) and deviations between simulated and measured output factors decreased to below 1 % and only for the smallest field size, deviations of up to 5 % were observed. In this study, however, both detectors were suitable for the whole range of the measured field sizes, which is also suggested by the good agreement of the values measured with these two detectors at larger field sizes. Therefore, the disagreement at the machine specific reference field size cannot be attributed to the detectors. Rather, it has to be attributed to a weakness of the MC calculation, most likely due to limitations of the developed phase space model (for discussion, see 4.2.4). On the other hand, the larger deviations at the smallest field size might result from alignment uncertainties in the measurements, which are critical for field size below 1 cm. This supposition complies with the finding that the measured values at the smallest field size were smaller than the calculated values. In addition, uncertainties in the implementation of the detector geometry in the MC simulation could contribute to the deviations at the smallest field size.

Besides deviation between measured and simulated values, also significant deviations between the two detectors were observed at the smallest field size. Existing literature has reported that for very small fields, with side of less than 1 cm, discrepancies exceeding 10 % can arise between the responses of air-filled and solid-state detectors [101]–[104]. There are several factors that influence the detector response in the small fields, leading to the observed differences in the output factors. These include: (i) volume averaging if the sensitive volume of the detector is larger than the uniform dose region of the small field, (ii) perturbations of the charged particle fluence by the detector, presumed to be mostly due to mass density differences to water [101], [105], and in magnetic fields (iii) the effect of the magnetic fields may have an additional influence.

Although both PinPoint 3D and microDiamond detectors have small sensitive volumes, the volume effect becomes pronounced for small field sizes, leading to an underestimation of absorbed dose. This effect should be more pronounced for PinPoint 3D detector as it has larger sensitive volume in comparison with microDiamond detector. Additionally, the density difference between the detector material and water perturbs the charged particle fluence. Here, not only the material of the sensitive volume matters but also the surrounding material of detector components [106], [107]. This perturbation effect is field size dependent and becomes significant in the small fields [108]. Generally, high-density detectors over-respond, while low-density detectors under-respond [109] [100]. In this study, it is therefore expected that the microDiamond as a solid-state detector will over-respond while the PinPoint 3D with air sensitive

volume will under-respond. The interplay of all these effects leads to larger deviations in output factors for the smallest field size measured with two detector types. Hence, the utilization of output correction factors becomes imperative for accurate determination of field output factors in such small fields, as no single detector can ensure precise dose determination without these corrections.

Output corrections factors in TRS-483 are tabulated as a function of the S_{eq} . Therefore, in this study, the calculation of S_{eq} was performed for each rectangular field and output factors were also presented as a function of S_{eq} . This approach was also employed for the nominally squared fields, since the actually measured FWHM in X and Y direction were not exactly the same. For the calculation of the S_{eq} the literature suggests two different formulas - equation (2.28) for the small fields and equation (2.29) for the larger fields. According to the TRS-483, the formula for small fields is recommended to be employed within the condition of $0.7 < X/Y < 1.4$ when presenting output correction factors. For rectangular fields falling outside this condition, it is advised to account for a higher level of uncertainty in the output correction factors [49]. In this study, a wide range of rectangular fields was investigated including elongated fields characterized by one side having a broad dimension and the other side having a small dimension, e.g. (9.96 x 0.83) cm². Therefore, both equations were utilized to compare output factors of different rectangular fields resulting in the output factor curve for square fields, as presented in Figure 3.11. For elongated rectangular fields that do not fulfil the condition for using the formula for small fields, the difference from S_{eq} obtained by the formula for large fields and small fields was up to 89.7 %. In cases where the condition was fulfilled, this difference was limited to 1.1 %. Given the overall better alignment with the square output factor curve when using the equation for large fields, the calculation of S_{eq} was consistently performed using the formula for large fields.

Output factors for off-axis fields were obtained by shifting the detector off-axis while measuring at the center of the field. The ratio of detector readings for off-axis fields refers to the machine-specific reference fields that were shifted by the same distance and in the same direction as the small field. Figure 3.13 provides a comparison of four output factor curves for square off-axis fields, which were shifted from the isocenter by 5 cm in four different directions. The observed deviation of off-axis output factors from their corresponding isocentric output factors was generally low. For PinPoint 3D this deviation was within 1 %, except for the smallest field size where deviation reached 3.8 %. For microDiamond measurements the deviation was even lower, staying within 0.8 % for all field sizes except the smallest one, where the deviation reached 2.4 %.

Output factor curves corresponding to each of the four off-axis positions were also independently compared using the two detectors. Each output factor value is presented in

Figure 3.14 as a function of S_{eq} . The S_{eq} value is determined from profile measurements conducted with the same detector that was utilized for the output factor measurements. The observed trends indicate that the detectors exhibit similar behavior in comparison to the isocentric position, presented in Figure 3.11. Notably, the microDiamond detector consistently displayed an over-response for the smallest field size in comparison to the PinPoint chamber,

reaching nearly 7 %. At the field size of $1.66 \times 1.66 \text{ cm}^2$, the agreement between the two detectors was best ($<1 \%$) across all measurement positions. However, for the larger field sizes, the behavior of the detectors reversed; microDiamond under-responded in comparison to PinPoint 3D.

4.2.4 Output correction factors

To establish detector-specific output correction factors for the 0.35 T MR-Linac, a combination of measured detector reading ratios (output factors) and MC simulated dose ratios was employed. This approach followed the formulation outlined in equation (2.34) and was applied for PinPoint 3D and microDiamond detectors covering various small square sizes. The resulting output correction factors were then presented as a function of S_{eq} obtained from profile measurements. It is important to note that the same detector was used for measuring the output factor and the lateral beam profile.

For the MC simulations, a phase space model of the ViewRay MRIdian device, as described in section 2.4.2., is required. With this respect, however, no device-specific information could be obtained from the vendor. Therefore, the project partners at the NPL developed an own phase space model of the ViewRay MRIdian device based on the publicly available documentation and research papers. The PDDs and lateral dose profiles measured in this thesis were used to test and adjust this model. Fine-tuning of the source model for each field size was performed by adjusting the energy and MLC openings to match measured PDDs and lateral dose profiles. Consequently, the model unavoidably incorporates several assumptions and approximations.

The field output correction factors, simulated at NPL on the basis of the optimized phase space file, were in turn provided for this thesis to convert measured output factors into output correction factors according to equation (2.34). With this respect, it is important to acknowledge that MC simulations were conducted using a simplified beam line model of the Viewray machine, which in turn introduces some uncertainties to the derived output correction factors.

As displayed in Figure 3.11, there was a disagreement between the measured and calculated output factors when normalizing to the machine specific reference field size f_{msr} , and normalizing to an intermediate field size f_{int} instead, resulted in a much better agreement. When the output correction factors were determined with the latter normalization, the agreement between solely calculated values and those obtained from the simulated dose ratios and the measured detector reading ratios improved accordingly for smaller field sizes. The remaining deviation at the machine specific reference field size is likely to be an issue with the accuracy of the MC at this field size. A potential reason could be additional scattering contributions from the Linac head at this large collimator aperture, which may not be accounted for in the adjustment of the phase space model by means of relative lateral and depth dose profiles. This hypothesis,

however, has not been investigated in this thesis and for a validation, further investigations are therefore required.

According to TRS 483, the field output factor with respect to the machine specific reference field can be split in two factors according to

$$\frac{D_{w,\vec{B},Q_{clin}}^{f_{clin}}}{D_{w,\vec{B},Q_{msr}}^{f_{msr}}} = \left[\frac{M_{\vec{B},Q_{clin}}^{f_{clin}}}{M_{\vec{B},Q_{int}}^{f_{int}}} k_{\vec{B},Q_{clin},Q_{int}}^{f_{clin},f_{int}} \right]_{det1} \left[\frac{M_{\vec{B},Q_{int}}^{f_{int}}}{M_{\vec{B},Q_{msr}}^{f_{msr}}} k_{\vec{B},Q_{int},Q_{msr}}^{f_{int},f_{msr}} \right]_{det2}, \quad (4.1)$$

where the first factor describes the transition of the field output factor from the small to the intermediate field and the second factor the transition from the intermediate to the machine specific reference field size. In contrast to TRS 483, the factors in (4.1) are referring to the presence of a magnetic field.

Since the results of the MC calculation at f_{msr} size are considered uncertain, only $k_{\vec{B},Q_{clin},Q_{int}}^{f_{clin},f_{int}}$ is reliable while $k_{\vec{B},Q_{int},Q_{msr}}^{f_{int},f_{msr}}$ remains uncertain due to the inconsistency of measurements and simulations at the machine specific reference field size. Since both intermediate and machine specific reference fields are relatively large, it is likely that the respective output factor correction is very small. This is in-line with the corrections obtained solely by MC simulations.

Finally, as for the output factors, the deviations of the corrections between measurements and simulations at the smallest field size may be attributed to potential uncertainties in the detector alignment as well as to uncertainties in the implementation of small details of the detector geometry in the MC simulation.

It should be noted that the derived correction factors depend not only on field size, but also on additional factors associated with the detector (as explained in section 4.2.3), as well as the detector orientation [17], [110], [111]. Therefore, the values of output correction factors presented in this work can be applied only to the investigated detectors if they were used in the same orientation relative to the beam to the magnetic field as in this study. A study by De Poorter et al. [57] recommends aligning cylindrical chambers in parallel to the magnetic field as this orientation minimizes magnetic field corrections.

This study demonstrated that both, PinPoint 3D and microDiamond detectors could be effectively used in dosimetry for small fields even in the presence of a 0.35 T magnetic field with appropriate use of the detector-specific correction factors. The specific values of $k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$ and $k_{\vec{B},Q_{clin},Q_{int}}^{f_{clin},f_{int}}$ for square fields are provided in Table A.3 in appendix . The maximum deviation of $k_{\vec{B},Q_{clin},Q_{msr}}^{f_{clin},f_{msr}}$ from unity was found to be $(3.05 \pm 0.11) \%$ and $(9.03 \pm 0.08) \%$ for the PinPoint 3D and the microDiamond detectors respectively, for the smallest square field size of $(0.82 \times 0.83) \text{ cm}^2$. For

the same field size, the deviation of $k_{\vec{B}, Q_{clin}, Q_{int}}^{f_{clin}, f_{int}}$ from unity was found to be $(0.64 \pm 0.16) \%$ and $(7.28 \pm 0.13) \%$ for the PinPoint 3D and the microDiamond detectors respectively.

Future work should focus on the development of a more precise MC beam model to reduce the uncertainty of the MC simulations and to enhance the dose determination accuracy. Additionally, alternative methods for determination of $k_{\vec{B}, Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$ should be explored, such as employing a reference detector with magnetic field-independent responses across field sizes. With this respect, Alanine dosimeters may be a promising reference detector for measuring field output factors in magnetic fields. In combination with output factors measured by other detectors, this approach may be used to determine $k_{\vec{B}, Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$ for those specific detectors.

5 Conclusion

In this work, dosimetry in presence of magnetic fields for MRgRT was investigated for photon and carbon-ion therapy. As ion-beam MRgRT is lagging behind photon beam MRgRT, one part of the project focused on reference dosimetry for carbon-ions in presence of magnetic fields. Since MRgRT with photon beams is already clinically established, the second part of the project went one step beyond and investigated dosimetry of small fields in the presence of magnetic fields.

Carbon-ion reference dosimetry in magnetic fields

The Farmer-type chamber (PTW 30013) response was experimentally investigated across magnetic flux densities from 0 T to 1 T for carbon-ion beam energies of 390.75 MeV/u and 200.28 MeV/u. Small, but significant change in the response, influenced by magnetic fields, was observed. No significant effect of the magnetic field was observed on the polarity and ion recombination correction factor for the same chamber.

Additionally, to explore the influence of chamber volume on the response change within magnetic fields, the same experiment was performed with five additional custom-made chambers of the same design as commercial PTW 30013, but with varying inner radii. The response of all six chambers was affected by the magnetic field, with the magnitude of the effect varying according to the magnetic flux density and chamber volume. As the chamber radius increased, the magnetic flux density at the largest change of the detector response was shifted to lower values. These experimental findings were validated with Monte Carlo simulations, where the responses of six chambers in magnetic fields were simulated after excluding the dead volume from the sensitive volume of the chambers.

The magnetic field had no significant effect on the local dose change. Therefore, the final magnetic field correction factor $k_{\vec{B},Q}$ is strongly dominated by the change in the chamber response. For the commercially available PTW 30013 chamber, the $k_{\vec{B},Q}$ correction was found to be up to 0.4 %. Although the overall effect is small, detector response changes were observed for all six chambers and for accurate dose measurements, appropriate corrections should be applied.

Future measurements should investigate additional detectors and magnetic field orientation. To gain a deeper understanding of the underlying reasons for the chamber response alteration in magnetic fields, more detailed Monte Carlo simulations of the secondary electron transport between the sensitive and dead detector volume are required.

Small photon field dosimetry in the presence of a magnetic field

The measurements conducted in small fields using the PinPoint 3D (PTW 31022) and the microDiamond (PTW 60019) detectors demonstrated a high level of reproducibility. Repeated measurements taken on different days underscored the reliability of the measurement setup and alignment procedure. The results for PinPoint3D detector showed that ion recombination and polarity corrections were independent of field size.

Lateral profile measurements carried out with both detectors indicated a slightly wider Y-profile compared to the X-profile. Differences between isocenter and maximum position of the profile were negligible for square isocentric fields in 0.35 T magnetic field. Profile measurements were extended to rectangular isocentric and squared off-axis fields. Overall, a good agreement below 1% was observed when comparing off-axis field sizes to the corresponding isocentric square field sizes, across the measured fields.

Output factor measurements for square fields were conducted at the isocenter rather than maximum position of each field, as this shift was not significant. Isocentric output factors referred to a machine-specific reference field, while output factors for off-axis square fields referred to a machine-specific reference fields shifted by the same distance and in the same direction as the small field. For converting rectangular fields into equivalent square field sizes two different formulas were tested - one recommended for large fields and another for small fields. Output factors for rectangular isocentric fields, determined as a function of equivalent square field size, aligned with those of square isocentric fields for both formulas. However, the formula designed for broad fields performed better for elongated rectangular fields. Output factors for square fields did not change significantly when the center of the field was 5 cm off-axis in cross-plane and in-plane direction.

The conversion of measured output factors into output correction factors was performed by Monte Carlo simulations of the dose for small and machine-specific reference fields. The corrections ranged up to 3 % for PinPoint 3D and up to 9 % for microDiamond detector when using the machine specific reference field and up to 0.6 % and 7 %, respectively, when using the intermediate field for normalization. For accurate dose measurements in presence of magnetic fields, it is necessary to apply these output correction factors for both detectors.

It is important to note that the presented correction values are preliminary. Further investigations and consistency checks with data derived by different methods and investigators are necessary before the data can be used clinically.

Appendix

Table A.1 Measured $k_{\vec{B},M,Q}$ values with corresponding standard error of the mean for the six chambers, along with applied statistical analysis: p-values for Shapiro-Wilk test and Student's t-test. P-values below significance level of 0.05 for the Student's t-test are displayed in bold.

chamber	B [T]	# measurements	$k_{\vec{B},M,Q}$	σ	Shapiro-Wilk test p-value	Student's t test p-value
R1	0.0	21	1.0000	0.0004	0.779	-
	0.1	9	1.0003	0.0007	0.827	0.374
	0.2	9	1.0007	0.0010	0.894	0.016
	0.3	9	1.0031	0.0008	0.821	≤0.001
	0.4	9	1.0036	0.0010	0.919	≤0.001
	0.5	9	1.0040	0.0005	0.815	≤0.001
	0.6	9	1.0045	0.0004	0.885	≤0.001
	0.7	9	1.0043	0.0008	0.746	≤0.001
	0.8	9	1.0054	0.0011	0.808	≤0.001
	0.9	9	1.0038	0.0005	0.637	≤0.001
	1.0	9	1.0051	0.0011	0.994	≤0.001
R2	0.0	21	1.0000	0.0004	0.100	-
	0.1	9	1.0014	0.0011	0.260	0.039
	0.2	9	1.0019	0.0008	0.354	0.016
	0.3	9	1.0045	0.0007	0.152	0.002
	0.4	9	1.0036	0.0011	0.129	0.012
	0.5	9	1.0043	0.0007	0.142	0.016
	0.6	9	1.0036	0.0015	0.157	0.031
	0.7	9	1.0027	0.0016	0.152	0.001
	0.8	9	1.0010	0.0007	0.200	0.016
	0.9	9	1.0010	0.0005	0.062	0.815
	1.0	9	1.0011	0.0009	0.085	0.598
R3	0.0	31	1.0000	0.0010	0.365	-
	0.1	19	1.0015	0.0008	0.348	≤0.001
	0.2	19	1.0042	0.0011	0.641	≤0.001
	0.3	19	1.0040	0.0008	0.061	≤0.001
	0.4	19	1.0035	0.0011	0.607	≤0.001
	0.5	19	1.0030	0.0011	0.480	≤0.001
	0.6	19	1.0015	0.0008	0.400	0.025
	0.7	19	0.9999	0.0011	0.151	0.608
	0.8	19	0.9991	0.0008	0.748	0.040
	0.9	19	1.0002	0.0008	0.424	0.883
	1.0	19	0.9999	0.0009	0.811	0.809

chamber	B [T]	# measurements	$k_{\bar{B},M,Q}$	σ	Shapiro- Wilk test p -value	Student's t test p -value
R4	0.0	21	1.0000	0.0010	0.935	-
	0.1	9	1.0014	0.0014	0.893	0.016
	0.2	9	1.0030	0.0008	0.220	0.025
	0.3	9	1.0028	0.0012	0.705	0.019
	0.4	9	1.0010	0.0015	0.332	0.158
	0.5	9	1.0012	0.0013	0.503	0.158
	0.6	9	0.9999	0.0012	0.112	0.725
	0.7	9	1.0003	0.0011	0.085	0.643
	0.8	9	0.9984	0.0011	0.414	0.026
	0.9	9	0.9998	0.0010	0.304	0.830
	1.0	9	1.0006	0.0009	0.484	0.815
R5	0.0	27	1.0000	0.0019	0.862	-
	0.1	9	1.0059	0.0022	0.518	0.004
	0.2	9	1.0062	0.0022	0.843	≤ 0.001
	0.3	9	1.0046	0.0020	0.603	0.002
	0.4	9	1.0030	0.0018	0.328	0.019
	0.5	9	1.0048	0.0023	0.519	0.023
	0.6	9	1.0031	0.0017	0.505	0.007
	0.7	9	1.0044	0.0015	0.760	0.014
	0.8	9	1.0034	0.0020	0.363	0.039
	0.9	9	1.0005	0.0020	1.000	0.116
	1.0	9	1.0023	0.0015	0.991	0.315
R6	0.0	15	1.0000	0.0006	0.708	-
	0.1	9	1.0054	0.0014	0.763	≤ 0.001
	0.2	9	1.0058	0.0014	0.601	≤ 0.001
	0.3	9	1.0045	0.0010	0.740	≤ 0.001
	0.4	9	1.0040	0.0009	0.865	0.003
	0.5	9	1.0022	0.0017	0.900	0.041
	0.6	9	1.0010	0.0007	0.681	0.056
	0.7	9	1.0016	0.0007	0.547	0.005
	0.8	9	1.0008	0.0010	0.958	0.164
	0.9	9	1.0009	0.0012	0.784	0.002
	1.0	9	0.9984	0.0008	0.801	0.518

Table A.2 The magnetic field correction factor $k_{\vec{B},Q}$ for six Farmer-type chambers (R1-R6) obtained by multiplying the measured $k_{\vec{B},M,Q}$ factor and the simulated $c_{\vec{B}}$ factor. The maximum $k_{\vec{B},Q}$ value for each chamber is displayed in bold.

chamber	R1		R2		R3		R4		R5		R6	
B [T]	$k_{\vec{B},Q}$	σ	$k_{\vec{B},Q}$	σ	$k_{\vec{B},Q}$	σ	$k_{\vec{B},Q}$	σ	$k_{\vec{B},Q}$	σ	$k_{\vec{B},Q}$	σ
0.0	1.0000	0.0004	1.0000	0.0004	1.0000	0.0010	1.0000	0.0010	1.0000	0.0019	1.0000	0.0006
0.1	1.0004	0.0007	1.0016	0.0011	1.0017	0.0008	1.0015	0.0014	1.0060	0.0022	1.0056	0.0014
0.2	1.0004	0.0010	1.0016	0.0008	1.0039	0.0011	1.0028	0.0008	1.0060	0.0022	1.0055	0.0014
0.3	1.0031	0.0008	1.0045	0.0007	1.0040	0.0008	1.0028	0.0012	1.0046	0.0020	1.0045	0.0010
0.4	1.0036	0.0010	1.0036	0.0011	1.0035	0.0011	1.0010	0.0015	1.0030	0.0018	1.0040	0.0009
0.5	1.0040	0.0005	1.0042	0.0007	1.0030	0.0011	1.0011	0.0013	1.0047	0.0023	1.0021	0.0017
0.6	1.0045	0.0004	1.0036	0.0015	1.0015	0.0008	0.9999	0.0012	1.0031	0.0017	1.0010	0.0007
0.7	1.0042	0.0008	1.0026	0.0016	0.9999	0.0011	1.0002	0.0011	1.0043	0.0015	1.0015	0.0007
0.8	1.0054	0.0011	1.0010	0.0007	0.9991	0.0008	0.9984	0.0011	1.0034	0.0020	1.0008	0.0010
0.9	1.0036	0.0005	1.0008	0.0005	1.0000	0.0008	0.9996	0.0010	1.0003	0.0020	1.0007	0.0012
1.0	1.0049	0.0011	1.0010	0.0009	0.9997	0.0009	1.0004	0.0009	1.0021	0.0015	0.9982	0.0008

Table A.3 Output correction factors with standard error of the mean for square isocentric fields for PinPoint 3D and microDiamond detectors normalized to the machine-specific reference field and to an intermediate field size of (3.32 x 3.32) cm². These values were determined from measured output factors and simulated dose ratios.

Nominal Field Size		$k_{\vec{B}, Q_{\text{clin}}, Q_{\text{msr}}}^{f_{\text{clin}}, f_{\text{msr}}}$		$k_{\vec{B}, Q_{\text{clin}}, Q_{\text{int}}}^{f_{\text{clin}}, f_{\text{int}}}$	
X [cm]	Y [cm]	PinPoint 3D	microDiamond	PinPoint 3D	microDiamond
9.96	9.96	1.0000	1.0000	-	-
4.98	4.98	0.9742 ± 0.013	0.9790 ± 0.0008	-	-
3.32	3.32	0.9757 ± 0.012	0.9811 ± 0.0010	1.0000	1.0000
2.49	2.48	0.9712 ± 0.012	0.9768 ± 0.0007	0.9954 ± 0.017	0.9956 ± 0.0013
1.66	1.66	0.9773 ± 0.010	0.9681 ± 0.0009	1.0016 ± 0.016	0.9868 ± 0.0014
0.83	0.82	0.9695 ± 0.011	0.9097 ± 0.0008	0.9936 ± 0.016	0.9272 ± 0.0013

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Bibliography

- [1] G. M. Cooper, "The Development and Causes of Cancer," in *The Cell: A Molecular Approach*. 2nd edition, Sinauer Associates, 2000. Accessed: Aug. 29, 2023. [Online]. Available: <https://www.ncbi.nlm.nih.gov/books/NBK9963/>
- [2] S. P. Jackson and J. Bartek, "The DNA-damage response in human biology and disease," *Nature*, vol. 461, no. 7267, Art. no. 7267, Oct. 2009, doi: 10.1038/nature08467.
- [3] M. B. Barton, M. Frommer, and J. Shafiq, "Role of radiotherapy in cancer control in low-income and middle-income countries," *Lancet Oncol.*, vol. 7, no. 7, pp. 584–595, Jul. 2006, doi: 10.1016/S1470-2045(06)70759-8.
- [4] G. Delaney, S. Jacob, C. Featherstone, and M. Barton, "The role of radiotherapy in cancer treatment," *Cancer*, vol. 104, no. 6, pp. 1129–1137, 2005, doi: 10.1002/cncr.21324.
- [5] "Technical specifications of radiotherapy equipment for cancer treatment." <https://www.who.int/publications-detail-redirect/9789240019980> (accessed Aug. 22, 2023).
- [6] R. Baskar, K. A. Lee, R. Yeo, and K.-W. Yeoh, "Cancer and Radiation Therapy: Current Advances and Future Directions," *Int. J. Med. Sci.*, vol. 9, no. 3, pp. 193–199, Feb. 2012, doi: 10.7150/ijms.3635.
- [7] M. Elshaikh, M. Ljungman, R. Ten Haken, and A. S. Lichter, "Advances in Radiation Oncology," *Annu. Rev. Med.*, vol. 57, no. 1, pp. 19–31, 2006, doi: 10.1146/annurev.med.57.121304.131431.
- [8] C. Garibaldi *et al.*, "Recent advances in radiation oncology," *ecancermedicalscience*, vol. 11, p. 785, Nov. 2017, doi: 10.3332/ecancer.2017.785.
- [9] L. Beaton, S. Bandula, M. N. Gaze, and R. A. Sharma, "How rapid advances in imaging are defining the future of precision radiation oncology," *Br. J. Cancer*, vol. 120, no. 8, pp. 779–790, Apr. 2019, doi: 10.1038/s41416-019-0412-y.
- [10] E. B. Podgorsak, "TREATMENT MACHINES FOR EXTERNAL BEAM RADIOTHERAPY".
- [11] C. Ma *et al.*, "Flattening filter free in intensity-modulated radiotherapy (IMRT) – Theoretical modeling with delivery efficiency analysis," *Med. Phys.*, vol. 46, no. 1, pp. 34–44, 2019, doi: 10.1002/mp.13267.
- [12] S. D. Sharma, "Unflattened photon beams from the standard flattening filter free accelerators for radiotherapy: Advantages, limitations and challenges," *J. Med. Phys. Assoc. Med. Phys. India*, vol. 36, no. 3, pp. 123–125, 2011, doi: 10.4103/0971-6203.83464.
- [13] D. Georg, T. Knöös, and B. McClean, "Current status and future perspective of flattening filter free photon beams," *Med. Phys.*, vol. 38, no. 3, pp. 1280–1293, Mar. 2011, doi: 10.1118/1.3554643.
- [14] Podgorsak E. B., *Radiation Oncology Physics*. in Non-serial Publications. Vienna: INTERNATIONAL ATOMIC ENERGY AGENCY, 2005.
- [15] I. J. Das, G. X. Ding, and A. Ahnesjö, "Small fields: Nonequilibrium radiation dosimetry," *Med. Phys.*, vol. 35, no. 1, pp. 206–215, 2008, doi: 10.1118/1.2815356.
- [16] I. Méndez and B. Casar, "A novel approach for the definition of small-field sizes using the concept of superellipse," *Radiat. Phys. Chem.*, vol. 189, p. 109775, Dec. 2021, doi: 10.1016/J.RADPHYSICHEM.2021.109775.

- [17] B. Casar, E. Gershkevitch, I. Mendez, S. Jurković, and M. S. Huq, "A novel method for the determination of field output factors and output correction factors for small static fields for six diodes and a microdiamond detector in megavoltage photon beams," *Med. Phys.*, vol. 46, no. 2, pp. 944–963, Feb. 2019, doi: 10.1002/mp.13318.
- [18] T. Tessonier *et al.*, "Commissioning of Helium Ion Therapy and the First Patient Treatment With Active Beam Delivery," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 116, no. 4, pp. 935–948, Jul. 2023, doi: 10.1016/j.ijrobp.2023.01.015.
- [19] G. Kraft, "Tumor therapy with heavy charged particles," *Prog. Part. Nucl. Phys.*, vol. 45, pp. S473–S544, Jan. 2000, doi: 10.1016/S0146-6410(00)00112-5.
- [20] O. Jäkel, "Physical advantages of particles: protons and light ions," *Br. J. Radiol.*, vol. 93, no. 1107, p. 20190428, Mar. 2020, doi: 10.1259/bjr.20190428.
- [21] H. Tsujii and T. Kamada, "A Review of Update Clinical Results of Carbon Ion Radiotherapy," *Jpn. J. Clin. Oncol.*, vol. 42, no. 8, pp. 670–685, Aug. 2012, doi: 10.1093/jjco/hys104.
- [22] J. J. Wilkens and U. Oelfke, "Direct Comparison of Biologically Optimized Spread-out Bragg Peaks for Protons and Carbon Ions," *Int. J. Radiat. Oncol.*, vol. 70, no. 1, pp. 262–266, Jan. 2008, doi: 10.1016/j.ijrobp.2007.08.029.
- [23] C. P. Karger, O. Jäkel, H. Palmans, and T. Kanai, "Dosimetry for ion beam radiotherapy," *Phys. Med. Biol.*, vol. 55, no. 21, pp. R193–R234, Nov. 2010, doi: 10.1088/0031-9155/55/21/R01.
- [24] H. Herrmann, Y. Seppenwoolde, D. Georg, and J. Widder, "Image guidance: past and future of radiotherapy," *Radiol.*, vol. 59, no. Suppl 1, pp. 21–27, 2019, doi: 10.1007/s00117-019-0573-y.
- [25] J. Liang *et al.*, "The effect of image-guided radiation therapy on the margin between the clinical target volume and planning target volume in lung cancer," *J. Med. Radiat. Sci.*, vol. 61, no. 1, pp. 30–37, Feb. 2014, doi: 10.1002/jmrs.42.
- [26] C. Kurz *et al.*, "Medical physics challenges in clinical MR-guided radiotherapy," *Radiat. Oncol.*, vol. 15, no. 1, p. 93, May 2020, doi: 10.1186/s13014-020-01524-4.
- [27] M. Karlsson, M. G. Karlsson, T. Nyholm, C. Amies, and B. Zackrisson, "Dedicated Magnetic Resonance Imaging in the Radiotherapy Clinic," *Int. J. Radiat. Oncol.*, vol. 74, no. 2, pp. 644–651, Jun. 2009, doi: 10.1016/j.ijrobp.2009.01.065.
- [28] T. Bostel *et al.*, "MR-guidance – a clinical study to evaluate a shuttle- based MR-linac connection to provide MR-guided radiotherapy," *Radiat. Oncol. Lond. Engl.*, vol. 9, p. 12, Jan. 2014, doi: 10.1186/1748-717X-9-12.
- [29] T. Bostel *et al.*, "Prospective feasibility analysis of a novel off-line approach for MR-guided radiotherapy," *Strahlenther. Onkol.*, vol. 194, no. 5, pp. 425–434, May 2018, doi: 10.1007/s00066-017-1258-y.
- [30] M. J. Menten, A. Wetscherek, and M. F. Fast, "MRI-guided lung SBRT: Present and future developments," *Phys. Med.*, vol. 44, pp. 139–149, Dec. 2017, doi: 10.1016/j.ejmp.2017.02.003.
- [31] S. Mutic and J. F. Dempsey, "The ViewRay System: Magnetic Resonance-Guided and Controlled Radiotherapy," *Semin. Radiat. Oncol.*, vol. 24, no. 3, pp. 196–199, 2014, doi: 10.1016/j.semradonc.2014.02.008.
- [32] S. Klüter, "Technical design and concept of a 0.35 T MR-Linac," *Clin. Transl. Radiat. Oncol.*, vol. 18, pp. 98–101, Sep. 2019, doi: 10.1016/j.ctro.2019.04.007.

- [33] D. Winkel *et al.*, "Adaptive radiotherapy: The Elekta Unity MR-linac concept," *Clin. Transl. Radiat. Oncol.*, vol. 18, pp. 54–59, Sep. 2019, doi: 10.1016/j.ctro.2019.04.001.
- [34] B. W. Raaymakers *et al.*, "First patients treated with a 1.5 T MRI-Linac: Clinical proof of concept of a high-precision, high-field MRI guided radiotherapy treatment," *Phys. Med. Biol.*, vol. 62, no. 23, pp. L41–L50, Nov. 2017, doi: 10.1088/1361-6560/aa9517.
- [35] R. Kashani and J. R. Olsen, "Magnetic Resonance Imaging for Target Delineation and Daily Treatment Modification," *Semin. Radiat. Oncol.*, vol. 28, no. 3, pp. 178–184, Jul. 2018, doi: 10.1016/j.semradonc.2018.02.002.
- [36] O. Bohoudi *et al.*, "Fast and robust online adaptive planning in stereotactic MR-guided adaptive radiation therapy (SMART) for pancreatic cancer," *Radiother. Oncol.*, vol. 125, no. 3, pp. 439–444, Dec. 2017, doi: 10.1016/j.radonc.2017.07.028.
- [37] I. Wahlstedt *et al.*, "Gating has a negligible impact on dose delivered in MRI-guided online adaptive radiotherapy of prostate cancer," *Radiother. Oncol.*, vol. 170, pp. 205–212, May 2022, doi: 10.1016/j.radonc.2022.03.013.
- [38] S. B. Jiang, "Technical aspects of image-guided respiration-gated radiation therapy," *Med. Dosim.*, vol. 31, no. 2, pp. 141–151, Jun. 2006, doi: 10.1016/j.meddos.2005.12.005.
- [39] Y. Cervantes, J. Duchaine, I. Billas, S. Duane, and H. Bouchard, "Monte Carlo calculation of detector perturbation and quality correction factors in a 1.5 T magnetic resonance guided radiation therapy small photon beams," *Phys. Med. Biol.*, vol. 66, no. 22, p. 225004, Nov. 2021, doi: 10.1088/1361-6560/ac3344.
- [40] L. N. Burigo and B. M. Oborn, "Integrated MRI-guided proton therapy planning: Accounting for the full MRI field in a perpendicular system," *Med. Phys.*, vol. 49, no. 3, pp. 1853–1873, 2022, doi: 10.1002/mp.15398.
- [41] IAEA, "Absorbed Dose Determination in External Beam Radiotherapy. Technical Report Series No. 398," 398, 2000.
- [42] I. Meijsing *et al.*, "Dosimetry for the MRI accelerator: The impact of a magnetic field on the response of a Farmer NE2571 ionization chamber," *Phys. Med. Biol.*, vol. 54, no. 10, pp. 2993–3002, 2009, doi: 10.1088/0031-9155/54/10/002.
- [43] D. J. O'Brien, D. A. Roberts, G. S. Ibbott, and G. O. Sawakuchi, "Reference dosimetry in magnetic fields: formalism and ionization chamber correction factors," *Med. Phys.*, vol. 43, no. 8, pp. 4915–4927, Aug. 2016, doi: 10.1118/1.4959785.
- [44] C. K. Spindeldreier *et al.*, "Radiation dosimetry in magnetic fields with Farmer-type ionization chambers: determination of magnetic field correction factors for different magnetic field strengths and field orientations," *Phys. Med. Biol.*, vol. 62, no. 16, pp. 6708–6728, Aug. 2017, doi: 10.1088/1361-6560/aa7ae4.
- [45] V. N. Malkov and D. W. O. Rogers, "Monte Carlo study of ionization chamber magnetic field correction factors as a function of angle and beam quality," *Med. Phys.*, vol. 45, no. 2, pp. 908–925, 2018, doi: 10.1002/mp.12716.
- [46] S. Pojtinger, O. S. Dohm, R.-P. Kapsch, and D. Thorwarth, "Ionization chamber correction factors for MR-linacs," *Phys. Med. Biol.*, vol. 63, no. 11, p. 11NT03, Jun. 2018, doi: 10.1088/1361-6560/aac4f2.
- [47] B. Van Asselen *et al.*, "A formalism for reference dosimetry in photon beams in the presence of a magnetic field," *Phys. Med. Biol.*, vol. 63, no. 12, Jun. 2018, doi: 10.1088/1361-6560/aac70e.

- [48] L. de Prez *et al.*, “Direct measurement of ion chamber correction factors, kQ and kB, in a 7 MV MRI-linac,” *Phys. Med. Biol.*, vol. 64, no. 10, p. 105025, May 2019, doi: 10.1088/1361-6560/ab1511.
- [49] IAEA, “Dosimetry of Small Static Fields Used in External Beam Radiotherapy. An IAEA-AAPM International Code of Practice for reference and relative dose determination. Technical Report Series No. 483,” 2017.
- [50] M. Marot *et al.*, “Proton beam dosimetry in the presence of magnetic fields using Farmer-type ionization chambers of different radii,” *Med. Phys.*, vol. n/a, no. n/a, doi: 10.1002/mp.16368.
- [51] H. Fuchs, F. Padilla-Cabal, L. Zimmermann, H. Palmans, and D. Georg, “MR-guided proton therapy: Impact of magnetic fields on the detector response,” *Med. Phys.*, vol. 48, no. 5, pp. 2572–2579, 2021, doi: 10.1002/mp.14660.
- [52] H. Fuchs, P. Moser, M. Gröschl, and D. Georg, “Magnetic field effects on particle beams and their implications for dose calculation in MR-guided particle therapy,” *Med. Phys.*, vol. 44, no. 3, pp. 1149–1156, Mar. 2017, doi: 10.1002/mp.12105.
- [53] E.-E. A. of N. M. Institutes, “Traceable dosimetry for small fields in MR-guided radiotherapy,” *EURAMET*. <https://www.euramet.org/research-innovation/search-research-projects/details/project/traceable-dosimetry-for-small-fields-in-mr-guided-radiotherapy> (accessed Aug. 03, 2023).
- [54] F. H. Attix, *Introduction to radiological physics and radiation dosimetry*. in Physics textbook. Weinheim: Wiley-VCH, 2004.
- [55] H. Bethe, “Bremsformel für Elektronen relativistischer Geschwindigkeit,” *Z. Für Phys.*, vol. 76, no. 5, pp. 293–299, May 1932, doi: 10.1007/BF01342532.
- [56] F. Bloch, “Zur Bremsung rasch bewegter Teilchen beim Durchgang durch Materie,” *Ann. Phys.*, vol. 408, no. 3, pp. 285–320, 1933, doi: 10.1002/andp.19334080303.
- [57] J. de Pooter *et al.*, “Reference dosimetry in MRI-linacs: evaluation of available protocols and data to establish a Code of Practice,” *Phys. Med. Biol.*, vol. 66, no. 5, p. 05TR02, Mar. 2021, doi: 10.1088/1361-6560/ab9efe.
- [58] S. Pojtinger, “Dosimetry of Ionizing Radiation in Magnetic Fields,” Dissertation, Universität Tübingen, 2021. doi: 10.15496/publikation-58583.
- [59] A. J. E. Raaijmakers, B. W. Raaymakers, and J. J. W. Lagendijk, “Integrating a MRI scanner with a 6 MV radiotherapy accelerator: Dose increase at tissue-air interfaces in a lateral magnetic field due to returning electrons,” *Phys. Med. Biol.*, vol. 50, no. 7, pp. 1363–1376, Apr. 2005, doi: 10.1088/0031-9155/50/7/002.
- [60] A. Lühr, L. N. Burigo, S. Gantz, S. M. Schellhammer, and A. L. Hoffmann, “Proton beam electron return effect: Monte Carlo simulations and experimental verification,” *Phys. Med. Biol.*, vol. 64, no. 3, p. 035012, Jan. 2019, doi: 10.1088/1361-6560/aafab4.
- [61] A. J. E. Raaijmakers, *MR-guided radiotherapy: magnetic field dose effects*. Utrecht University, 2008.
- [62] “Technical Note: Experimental verification of magnetic field-induced beam deflection and Bragg peak displacement for MR-integrated proton therapy - Schellhammer - 2018 - Medical Physics - Wiley Online Library.” <https://aapm.onlinelibrary.wiley.com/doi/10.1002/mp.12961> (accessed May 24, 2023).

- [63] R. Wolf and T. Bortfeld, "An analytical solution to proton Bragg peak deflection in a magnetic field," *Phys. Med. Biol.*, vol. 57, no. 17, pp. N329–N337, Sep. 2012, doi: 10.1088/0031-9155/57/17/N329.
- [64] M. Akbari and A. Karimian, "Monte Carlo assessment of beam deflection and depth dose equivalent variation of a carbon-ion beam in a perpendicular magnetic field," *Phys. Med.*, vol. 61, pp. 33–43, May 2019, doi: 10.1016/j.ejmp.2019.04.016.
- [65] C. Eduardo De Almeida and C. Salata, "Absolute, Reference, and Relative Dosimetry in Radiotherapy," in *Dosimetry*, T. J. FitzGerald and M. Bishop-Jodoin, Eds., IntechOpen, 2022. doi: 10.5772/intechopen.101806.
- [66] F. M. Khan, *The physics of radiation therapy*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.
- [67] L. A. DeWerd and B. R. Smith, "Ionization Chamber Instrumentation," in *Radiation Therapy Dosimetry: A Practical Handbook*, A. Darafsheh, Ed., 1st ed. Names: Darafsheh, Arash, editor. Title: Radiation therapy dosimetry : a practical handbook / edited by Arash Darafsheh. Description: First edition. | Boca Raton : CRC Press, 2021.: CRC Press, 2021, pp. 19–30. doi: 10.1201/9781351005388-2.
- [68] J. W. Boag, "Distortion of the Electric Field in an Ionization Chamber due to a Difference in Potential between Guard Ring and Collector," *Phys. Med. Biol.*, vol. 9, no. 1, pp. 25–32, Jan. 1964, doi: 10.1088/0031-9155/9/1/302.
- [69] V. Malkov, "Charged Particle Transport in Magnetic Fields in the EGSnrc Monte Carlo Code System," Doctor of Philosophy, Carleton University, Ottawa, Ontario, 2018. doi: 10.22215/etd/2018-12637.
- [70] P. M. Rosenwald A. Nahum, J. C., Ed., *Handbook of Radiotherapy Physics: Theory and Practice*. Boca Raton: CRC Press, 2007. doi: 10.1201/9781420012026.
- [71] N. Makarova, "Handbook of radiotherapy physics", Accessed: May 16, 2023. [Online]. Available: https://www.academia.edu/36545225/Handbook_of_radiotherapy_physics
- [72] P. R. Almond *et al.*, "AAPM's TG-51 protocol for clinical reference dosimetry of high-energy photon and electron beams," *Med. Phys.*, vol. 26, no. 9, pp. 1847–1870, 1999, doi: 10.1118/1.598691.
- [73] J. W. Boag and J. Curren, "Current collection and ionic recombination in small cylindrical ionization chambers exposed to pulsed radiation," *Br. J. Radiol.*, vol. 53, no. 629, pp. 471–478, May 1980, doi: 10.1259/0007-1285-53-629-471.
- [74] D. J. O'Brien, J. Dolan, S. Pencea, N. Schupp, and G. O. Sawakuchi, "Relative dosimetry with an MR-linac: Response of ion chambers, diamond, and diode detectors for off-axis, depth dose, and output factor measurements: Response," *Med. Phys.*, vol. 45, no. 2, pp. 884–897, Feb. 2018, doi: 10.1002/mp.12699.
- [75] C. Legrand, G. H. Hartmann, and C. P. Karger, "Experimental determination of the effective point of measurement and the displacement correction factor for cylindrical ionization chambers in a 6 MV photon beam," *Phys. Med. Biol.*, vol. 57, no. 21, pp. 6869–6880, Nov. 2012, doi: 10.1088/0031-9155/57/21/6869.
- [76] S. E. Combs, O. Jäkel, T. Haberer, and J. Debus, "Particle therapy at the Heidelberg Ion Therapy Center (HIT) – Integrated research-driven university-hospital-based radiation oncology service in Heidelberg, Germany," *Radiother. Oncol.*, vol. 95, no. 1, pp. 41–44, Apr. 2010, doi: 10.1016/j.radonc.2010.02.016.

- [77] C. K. Spindeldreier, "Dosimetry with ionization chambers and optically stimulated luminescence detectors in magnetic fields," 2017.
- [78] P. Andreo, "Monte Carlo simulations in radiotherapy dosimetry," *Radiat. Oncol.*, vol. 13, no. 1, p. 121, Jun. 2018, doi: 10.1186/s13014-018-1065-3.
- [79] J. S. Verhaegen Frank, Ed., *Monte Carlo Techniques in Radiation Therapy*. Boca Raton: CRC Press, 2013. doi: 10.1201/b13961.
- [80] U. Fano, "Note on the Bragg-Gray cavity principle for measuring energy dissipation," *Radiat. Res.*, vol. 1, no. 3, pp. 237–240, Jun. 1954.
- [81] H. Bouchard, J. de Pooter, A. Bielajew, and S. Duane, "Reference dosimetry in the presence of magnetic fields: conditions to validate Monte Carlo simulations," *Phys. Med. Biol.*, vol. 60, no. 17, p. 6639, Aug. 2015, doi: 10.1088/0031-9155/60/17/6639.
- [82] I. Kawrakow, E. Mainegra-Hing, D. W. O. Rogers, F. Tessier, and B. R. B. Walters, "Monte Carlo Simulation of Electron and Photon Transport".
- [83] I. Kawrakow, "Accurate condensed history Monte Carlo simulation of electron transport. I. EGSnrc, the new EGS4 version," *Med. Phys.*, vol. 27, no. 3, pp. 485–498, 2000, doi: 10.1118/1.598917.
- [84] J. Perl, J. Shin, J. Schümann, B. Faddegon, and H. Paganetti, "TOPAS: An innovative proton Monte Carlo platform for research and clinical applications," *Med. Phys.*, vol. 39, no. 11, pp. 6818–6837, 2012, doi: 10.1118/1.4758060.
- [85] B. Faddegon *et al.*, "The TOPAS tool for particle simulation, a Monte Carlo simulation tool for physics, biology and clinical research," *Phys. Med.*, vol. 72, pp. 114–121, Apr. 2020, doi: 10.1016/j.ejmp.2020.03.019.
- [86] S. Agostinelli *et al.*, "Geant4—a simulation toolkit," *Nucl. Instrum. Methods Phys. Res. Sect. Accel. Spectrometers Detect. Assoc. Equip.*, vol. 506, no. 3, pp. 250–303, Jul. 2003, doi: 10.1016/S0168-9002(03)01368-8.
- [87] E. Poon, J. Seuntjens, and F. Verhaegen, "Consistency test of the electron transport algorithm in the GEANT4 Monte Carlo code," *Phys. Med. Biol.*, vol. 50, no. 4, pp. 681–694, Feb. 2005, doi: 10.1088/0031-9155/50/4/008.
- [88] V. N. Malkov and D. W. O. Rogers, "Charged particle transport in magnetic fields in EGSnrc: *B* fields in EGSnrc," *Med. Phys.*, vol. 43, no. 7, pp. 4447–4458, Jun. 2016, doi: 10.1118/1.4954318.
- [89] K.-S. Baumann, S. Kaupa, C. Bach, R. Engenhardt-Cabillic, and K. Zink, "Monte Carlo calculation of beam quality correction factors in proton beams using TOPAS/GEANT4," *Phys. Med. Biol.*, vol. 65, no. 5, p. 055015, Mar. 2020, doi: 10.1088/1361-6560/ab6e53.
- [90] M. Marot, F. Jäger, S. Greulich, C. P. Karger, O. Jaekel, and L. N. Burigo, "Monte Carlo simulation for proton dosimetry in magnetic fields: Fano test and magnetic field correction factors k_B for Farmer-type ionization chambers," *Phys. Med. Biol.*, Aug. 2023, doi: 10.1088/1361-6560/acefa1.
- [91] S. Pojtinger, R.-P. Kapsch, O. S. Dohm, and D. Thorwarth, "A finite element method for the determination of the relative response of ionization chambers in MR-linacs: simulation and experimental validation up to 1.5 T," *Phys. Med. Biol.*, vol. 64, no. 13, p. 135011, Jul. 2019, doi: 10.1088/1361-6560/ab2837.
- [92] B. K. Shukla *et al.*, "Dosimetry in magnetic fields with dedicated MR-compatible ionization chambers."

- [93] K. Smit, B. van Asselen, J. G. M. Kok, A. H. L. Aalbers, J. J. W. Lagendijk, and B. W. Raaymakers, "Towards reference dosimetry for the MR-linac: magnetic field correction of the ionization chamber reading," *Phys. Med. Biol.*, vol. 58, no. 17, p. 5945, Aug. 2013, doi: 10.1088/0031-9155/58/17/5945.
- [94] J. Vedelago, C. P. Karger, and O. Jäkel, "A review on reference dosimetry in radiation therapy with proton and light ion beams: status and impact of new developments," *Radiat. Meas.*, vol. 157, p. 106844, Sep. 2022, doi: 10.1016/j.radmeas.2022.106844.
- [95] H. Fuchs, F. Padilla-Cabal, B. M. Oborn, and D. Georg, "Commissioning a beam line for MR-guided particle therapy assisted by in-silico methods," *Med. Phys.*, Dec. 2022, doi: 10.1002/MP.16143.
- [96] S. Pojtinger *et al.*, "Experimental determination of magnetic field correction factors for ionization chambers in parallel and perpendicular orientations," *Phys. Med. Biol.*, vol. 65, no. 24, p. 245044, Dec. 2020, doi: 10.1088/1361-6560/abca06.
- [97] "BEAMSCAN | PTW." <https://www.ptwdosimetry.com/en/products/beamscan> (accessed Aug. 08, 2023).
- [98] L. Vieilleveigne and F. X. Arnaud, "Dosimetric performance of the new PTW 31022 PinPoint 3D ionization chamber in high energy photon beams," *Biomed. Phys. Eng. Express*, vol. 4, no. 4, p. 047002, Apr. 2018, doi: 10.1088/2057-1976/aabeef.
- [99] H. K. Looe *et al.*, "The polarity effect of compact ionization chambers used for small field dosimetry," *Med. Phys.*, vol. 45, no. 12, pp. 5608–5621, 2018, doi: 10.1002/mp.13227.
- [100] I. J. Das *et al.*, "Report of AAPM Task Group 155: Megavoltage photon beam dosimetry in small fields and non-equilibrium conditions," *Med. Phys.*, vol. 48, no. 10, pp. e886–e921, 2021, doi: 10.1002/mp.15030.
- [101] T. S. A. Underwood, B. C. Rowland, R. Ferrand, and L. Vieilleveigne, "Application of the Exradin W1 scintillator to determine Ediode 60017 and microDiamond 60019 correction factors for relative dosimetry within small MV and FFF fields," *Phys. Med. Biol.*, vol. 60, no. 17, p. 6669, Aug. 2015, doi: 10.1088/0031-9155/60/17/6669.
- [102] J. E. Morales, S. B. Crowe, R. Hill, N. Freeman, and J. V. Trapp, "Dosimetry of cone-defined stereotactic radiosurgery fields with a commercial synthetic diamond detector," *Med. Phys.*, vol. 41, no. 11, p. 111702, 2014, doi: 10.1118/1.4895827.
- [103] X. R. Zhu, J. J. Allen, J. Shi, and W. E. Simon, "Total scatter factors and tissue maximum ratios for small radiosurgery fields: Comparison of diode detectors, a parallel-plate ion chamber, and radiographic film," *Med. Phys.*, vol. 27, no. 3, pp. 472–477, 2000, doi: 10.1118/1.598915.
- [104] F. Sánchez-Doblado, G. H. Hartmann, J. Pena, J. V. Roselló, G. Russiello, and D. M. Gonzalez-Castaño, "A new method for output factor determination in MLC shaped narrow beams," *Phys. Med.*, vol. 23, no. 2, pp. 58–66, Jun. 2007, doi: 10.1016/j.ejmp.2007.03.002.
- [105] A. Ralston, M. Tyler, P. Liu, D. McKenzie, and N. Suchowerska, "Over-response of synthetic microDiamond detectors in small radiation fields," *Phys. Med. Biol.*, vol. 59, no. 19, p. 5873, Sep. 2014, doi: 10.1088/0031-9155/59/19/5873.
- [106] I. J. Das and P. Francescon, "Comments on the TRS-483 protocol on small field dosimetry," *Med. Phys.*, vol. 45, no. 12, pp. 5666–5668, 2018, doi: 10.1002/mp.13236.

- [107] P. Francescon, S. Cora, and N. Satariano, "Calculation of for several small detectors and for two linear accelerators using Monte Carlo simulations," *Med. Phys.*, vol. 38, no. 12, pp. 6513–6527, 2011, doi: 10.1118/1.3660770.
- [108] A. J. D. Scott, S. Kumar, A. E. Nahum, and J. D. Fenwick, "Characterizing the influence of detector density on dosimeter response in non-equilibrium small photon fields," *Phys. Med. Biol.*, vol. 57, no. 14, p. 4461, Jun. 2012, doi: 10.1088/0031-9155/57/14/4461.
- [109] H. Benmakhlouf and P. Andreo, "Spectral distribution of particle fluence in small field detectors and its implication on small field dosimetry," *Med. Phys.*, vol. 44, no. 2, pp. 713–724, 2017, doi: 10.1002/mp.12042.
- [110] J. Begg, U. Jelen, Z. Moutrie, C. Oliver, L. Holloway, and R. Brown, "ACPSEM position paper: dosimetry for magnetic resonance imaging linear accelerators," *Phys. Eng. Sci. Med.*, vol. 46, no. 1, pp. 1–17, 2023, doi: 10.1007/s13246-023-01223-w.
- [111] G. X. Ding *et al.*, "Impact of inhomogeneity corrections on dose coverage in the treatment of lung cancer using stereotactic body radiation therapy," *Med. Phys.*, vol. 34, no. 7, pp. 2985–2994, 2007, doi: 10.1118/1.2745923.

Personal contributions

Journal Articles

Marot M, **Surla S**, Burke E, Brons S, Runz A, Greilich S, Karger C P, Jäkel O and Burigo L N: "Proton beam dosimetry in the presence of magnetic fields using Farmer-type ionization chambers of different radii" *Medical Physics* 2023

Conference contributions

Surla S, Buchele C, Klüter S, Rhein B, Karger C P: "Reproducibility of dose measurements and influence of recombination and polarity correction for output factor measurements at a 0.35 T MR-Linac", *SGSMP, ÖGMP, DGMP, digital congress, 2021 (poster presentation)*

Marot M, **Surla S**, Brons S, Runz A, Greilich S, Karger C P, Jäkel O and Burigo L N: "Proton beam dosimetry in magnetic field using Farmer-type ionization chamber", *Société Française de Physique Médicale (SFPM), Lyon, France, 2021 (oral presentation)*

Marot M, **Surla S**, Runz A, Greilich S, Karger C P, Jäkel O and Burigo L N: "Proton beam dosimetry in magnetic field: Ionization chamber response", *DKFZ PhD poster presentation, Heidelberg, Germany, 2021 (poster presentation)*

Surla S, M. Marot, Brons S, Burigo L N and Karger C P: "Impact of magnetic field on the chamber response in carbon ion beam dosimetry", *PTCOG 60 Miami, USA, 2022 (poster presentation)*

Marot M, **Surla S**, Burke E, Brons S, Runz A, Greilich S, Karger C P, Jäkel O and Burigo L N: "Ionization chamber response to protons in presence of magnetic field", *PTCOG 60 Miami, USA, 2022 (oral presentation)*

Surla S, Klüter S, Renkamp C K, Buchele C, Rhein B, Karger C P: "Output factor measurements for small isocentric and off-axis photon fields at a 0.35 T MR-Linac", *9th MRinRT Symposium, Los Angeles, USA, 2023 (oral presentation)*

Marot M, **Surla S**, Burke E, Brons S, Jäger F, Runz A, Greilich S, Karger C P, Jäkel O and Burigo L N: "Measurements and Monte Carlo simulations of the response of a Farmer-type ionization chamber for proton beams in the presence of magnetic fields for the determination of k_B ", *9th MRinRT Symposium, Los Angeles, USA, 2023 (oral presentation)*

Surla S, M. Marot, Brons S, Burigo L N and Karger C P: "Impact of magnetic field on the chamber response in carbon ion beam dosimetry", *DKFZ PhD poster presentation, Heidelberg, Germany, 2023 (poster presentation)*

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Declaration

I, Sonja Surla, herewith declare that I have composed the present thesis myself and without use of any other than the cited sources and aids.

The thesis in has not been submitted to any examination body and has not been published.

Heidelberg, August 27th, 2023


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