

Design, development and validation of a novel ionization chamber for emerging hadron therapy modalities: FLASH proton therapy and carbon ion therapy

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Abstract

The limited effectiveness against radioresistant tumors and the radiation-induced toxicity in normal organs remain two major challenges to achieve optimal treatment outcomes in modern radiotherapy. Among advanced treatment modalities, high-LET particle therapy using heavy charged particles such as carbon ions induces dense ionization events along their tracks, enhancing biological effectiveness. More recently, FLASH radiotherapy has emerged as a promising technique that delivers radiation at ultra-high dose rates and has shown potential to spare normal tissues while maintaining tumor control. Accurate dosimetry is essential to ensure the safe and effective application of these modalities. However, the complex beam characteristics of high ionization densities and extreme dose rates introduce significant ion recombination losses in ionization chambers (ICs), the standard instruments for reference dosimetry. Among other challenges, when correcting for recombination losses, the established correction methodologies with current detector designs are complex, time-consuming and in some cases unreliable under these conditions. This thesis addresses different challenges associated with these advanced modalities by deepening the understanding of ion recombination and charge carrier transport processes in ICs, identifying radiation resistant materials for prolonged ultra-high dose rate (UHDR) and ultra-high dose per pulse (UHDP) operation, and developing a novel ionization chamber concept for reference dosimetry including its inherent method to correct for recombination losses. A Monte Carlo simulation framework was developed to model recombination efficiencies under realistic beam conditions beyond the limitations of theoretical models. Complementary experimental studies assessed the radiation tolerance of materials commonly used in ICs under high cumulative doses and varying dose rate conditions. Building on these insights, a dual gap ionization chamber (DGIC) prototype was designed, constructed, and tested across multiple beams. The DGIC allows straightforward determination of recombination correction factors from a single irradiation, resulting in a more time-efficient dosimetric workflow, while maintaining uncertainties comparable to those of currently endorsed methods.

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List of publications

Publications

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List of abbreviations

2VM		Two Voltage Method
3VM		Three Voltage Method
CM		Charge Multiplication
DGIC		Dual Gap Ionization Chamber
DPP		Dose Per Pulse
FEF		Free Electron Fraction
IAEA		International Atomic Energy Agency
IC		Ionization Chamber
LET		Linear Energy Transfer
LINAC		Linear Accelerator
MC		Monte Carlo
PBS		Pencil Beam Scanning
PDD		Percentage Depth Dose
PDE		Partial Differential Equation
PRF		Pulse Repetition Frequency
QA		Quality Assurance
RBE		Relative Biological Effectiveness
SCS		Space Charge Screening
SOBP		Spread Out Bragg Peak
SSD		Source to Surface Distance
TPS		Treatment Planning System
UHDP		Ultra High Dose per Pulse
UHDR		Ultra High Dose Rate
WET		Water Equivalent Thickness

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Chapter 1

Overview

This chapter presents the motivations underlying this thesis and provides an overview of its main contributions to the field, together with the overall structure of the thesis.

1.1 Research motivation

Radiotherapy is one of the principal modalities for cancer treatment, used either alone or in combination with surgery, chemotherapy, or other targeted therapies. The interaction of ionizing radiation with biological matter has been extensively studied, leading to the use of multiple radiation types and delivery techniques that optimize tumor control while minimizing damage to surrounding healthy tissues.

From the early use of X-rays, technological progress has enabled highly conformal dose delivery, allowing precise shaping of the radiation field to match tumor geometry. In recent decades, particle therapy (PT), including protons and heavier ions, has further improved dose conformity, offering superior sparing of healthy organs and, in some cases, increased biological effectiveness.

More recently, research has explored radiation modalities that combine excellent dose distribution with unique radiobiological advantages. High Linear Energy Transfer (LET) particles, such as carbon ions, not only maintain high dose conformity but also exhibit enhanced relative biological effectiveness (RBE), making them promising for the treatment of radioresistant tumors. The recent re-discovery of the FLASH effect, a still unknown biological mechanism observed at ultra-high dose rates (UHDR), has opened a new frontier in radiotherapy. Preclinical studies have shown that the FLASH effect can maintain tumor control while reducing normal tissue toxicity.

Radiotherapy relies on complex treatment machines that must meet strict quality and safety requirements. This is ensured in practice through dosimetric verifications, which include regular quality assurance (QA) measurements of machine output to ensure, for example, that the delivered dose matches the prescribed dose. The complexity of novel modalities such as carbon therapy and FLASH therapy introduces unique dosimetric challenges, particularly for ionization chambers (ICs), which remain the gold standard for reference dosimetry.

Under high-LET or UHDR conditions, ionization chambers experience significant ion recombination losses due to the high density of ions created in very small spatial and temporal scales. This reduces collection efficiency and requires the application of a correction factor that may depend on the specific beam properties and chamber design. While several theoretical models exist to describe ion recombination, they may fail under certain irradiation conditions, as their assumptions may not hold for advanced modalities. Experimental determination of recombination correction factors is therefore recommended.

Under these advanced treatment modalities periodic determination of recombination correction factors is often impractical, as existing methods can be too time-consuming or incompatible with routine QA workflows. Consequently, these factors may remain unverified for extended periods, potentially affecting dosimetric accuracy. Beyond recombination issues, other practical challenges also arise, such as the degradation of conventional ionization chambers under prolonged UHDR exposure, which can compromise detector performance and longevity.

The present thesis addresses these challenges by further understanding fundamental ion recombination and transport processes in ICs, identifying suitable materials for prolonged UHDR irradiation, and designing and testing a novel ionization chamber specifically tailored for reference dosimetry in advanced treatment modalities. The primary aim is to develop a detector that simplifies the determination of ion recombination correction factors while maintaining accuracy across a wide range of beam radiation types and temporal structures.

1.2 Main contributions

This thesis is structured around three research papers: two preparatory studies intended to guide the optimal design of the detector, and a third that presents the development and testing of the final prototype.

1.2.1 Modeling recombination and ion transport in ICs

Although ICs have been used in dosimetry for decades, conventional reference conditions permit simplifying assumptions about charge collection and recombination. These assumptions no longer hold for modern modalities, where large LET and dose rates cause other non-negligible effects. In this work, an open-source Monte Carlo simulation tool was developed to model ion transport and recombination processes under more realistic irradiation conditions. This tool enables detailed study of correction factor dependencies on chamber geometry, gap size, and multiple beam parameters, and has been used to optimize the chamber design developed in this thesis.

1.2.2 Identifying materials for prolonged UHDR irradiations

Clinical translation of FLASH therapy will inevitably require prolonged UHDR exposures, during which dosimeters can accumulate very high total doses. To ensure the longevity and stability of dosimetric devices, a systematic study of materials used in IC construction and phantoms was conducted. Candidate materials were irradiated with both electrons and protons under various conditions, including different cumulative doses, average dose rates, and instantaneous dose rates.

Their physical, chemical, and mechanical properties were monitored over time to assess radiation-induced degradation or recovery. This work identifies suitable materials for durable detector construction in high dose and UHDR environments that are needed for the development of the IC prototype.

1.2.3 Development and testing of a novel IC design

Building on the findings from the simulation and material studies, a novel dual-gap ionization chamber (DGIC) was designed for reference dosimetry in advanced modalities. This design enables direct determination of recombination correction factors by exploiting the variation in the measured charge ratio between the two gaps from a single irradiation, thereby improving accuracy and compatibility with clinical workflows. Several iterations of the prototype were built and evaluated, resulting in a final optimized design. This chapter presents the results for the final design, which was tested across a wide range of beam types and delivery modes, including a carbon ion beam, an UHDR proton beam, and, the most extreme case, an ultra-high dose per pulse (UHDP) electron beam.

1.3 Thesis outline

The thesis is structured as follows:

- Chapter 1: Which is the present chapter, it resumes the motivations behind this thesis and provides an overview of the thesis contributions to the field.
- Chapter 2: Provides the theoretical background necessary for the thesis. It covers the basic principles of radiotherapy, introduces the rationale behind novel treatment techniques such as particle therapy and FLASH, and reviews the fundamentals of reference dosimetry, ionization chamber operation and ion recombination.
- Chapter 3: Describes the development of an in-house Monte Carlo simulation to model ion transport and recombination processes in ionization chambers. The chapter presents the validation of the model against existing theories and experimental data.
- Chapter 4: Reports on the experimental study of different materials exposed to prolonged UHDR conditions. This includes the irradiation protocols, characterization methods, and assessment of material performance, and concludes on recommendations of commonly used materials for constructing dosimetric devices for UHDR applications.

-
- Chapter 5: Details the design, development, and experimental evaluation of the proposed prototype: a dual-gap ionization chamber (DGIC). It covers the operating principle, optimization process, and performance testing across multiple beam types and delivery modes.
 - Chapter 6: Summarizes the findings of the thesis, discusses their implications for clinical practice and future research, and provides concluding remarks from a personal perspective.

Chapter 2

Introduction

This chapter provides the theoretical background relevant to this thesis, covering the fundamental principles of radiotherapy, the rationale for advanced techniques and the fundamentals of reference dosimetry, with a particular emphasis on ionization chambers and a detailed focus on ion recombination.

2.1 Radiotherapy

Cancer is one of the leading causes of death globally, with an estimated 20 million new cases and 9.7 million deaths reported in 2022. According the World Health Organization (WHO) [83], the global cancer incidence is projected to rise to nearly 35 million cases annually by 2050, driven largely by population ageing and lifestyle-related factors [191]. In industrialized countries, radiotherapy (RT) is widely integrated into cancer care, as it is estimated that over 50% of cancer patients receive RT at some point during the course of their disease [15].

The primary objective of radiotherapy is to eradicate malignant cells by inducing irreparable DNA damage with ionizing radiation, while sparing surrounding healthy tissues to avoid acute and late toxicities. Achieving this delicate balance requires accurate dose delivery and careful consideration of normal tissue tolerance and tumor biology. In RT clinical practice, the oncologist prescribes the dose (the mean energy imparted per unit mass) that achieves tumor control while respecting tolerance thresholds for surrounding healthy tissues.

The use of radiation for cancer treatment dates back to shortly after Röntgen's discovery of X-rays in 1895 [160]. Since then, radiotherapy has evolved from rudimentary X-ray tubes to highly sophisticated treatment systems. Today, a variety of radiation types are used clinically, including photons, electrons, protons, and heavier ions, each with distinct physical properties and biological effectiveness [120, 140].

The following sections introduce key concepts related to the physics of particle-matter interactions, radiobiological effects, beam delivery technologies and their relevance to radiotherapy. These provide the necessary background on reference dosimetry as well as the rationale and specific challenges to novel radiotherapy modalities, which are central to the scope of this thesis.

2.2 Interaction of ionizing radiation with matter

There are different types of ionizing radiation that are used with radiotherapeutic fines, depending on their interaction with matter different properties and deposition of energy are observed:

2.2.1 Non-charged particles

Photons are by far the most widely used non-charged particle in external beam RT. Because they carry no electric charge, photons can travel considerable dis-

tances through matter before interacting with atomic structures [120]. The nature and probability of these interactions depends strongly on their energy.

At low photon energies, scattering processes such as Thomson and Rayleigh scattering may occur, involving the deflection of the incident photon with negligible energy transfer to the medium. As photon energy increases, three principal mechanisms become dominant: the photoelectric effect, where the photon is fully absorbed and an atomic electron is ejected; Compton scattering, in which the photon transfers part of its energy to an atomic electron and is deflected with reduced energy; and pair production, where the photon is converted into an electron–positron pair in the vicinity of a nucleus [12].

The attenuation of a photon beam as it passes through matter is described by the exponential attenuation law [180]:

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

Where $I(x)$ is the photon beam intensity after traversing a thickness x (in cm) of material, I_0 is the initial intensity and μ (in cm^{-1}) is the linear attenuation coefficient. This coefficient represents the probability per unit length that a photon interacts with the medium and is given from the contribution of the previously described interaction mechanisms.

Since μ depends both on the material composition and its density, the mass attenuation coefficient μ/ρ (in $\text{cm}^2 \text{g}^{-1}$) is often used to remove the influence of density alone. The variation of this coefficient with photon energy, and the relative contribution of each interaction process is illustrated in Figure 2.1.

X-rays produced in the megavoltage (MV) range typical of clinical radiotherapy, Compton scattering and pair production predominate [55]. Both processes produce energetic secondary electrons which undergo further ionizations in the surrounding medium. These secondary electrons with relative long range (1.5 cm in water for a 6 MV photon beam) are mainly responsible for the actual deposition of energy in matter and cause a shift between the position of photon interaction and that of energy deposition in the material. This shift causes the build-up effect [151]: an increase in the dose deposited in the first centimeters of the beam's path through the material. The dose rises until it reaches a maximum, where charged particle equilibrium is reached (the number and energy of charged particles entering a small volume equal those leaving it), followed by the characteristic exponential decrease shown in Figure 2.2 for therapeutic X-rays and ^{60}Co .

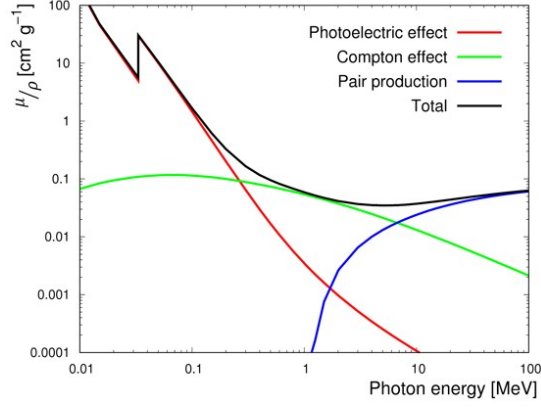


Figure 2.1: Contributions of Photoelectric effect, Compton effect, and Pair production to the mass attenuation coefficient as a function of photon energy. Figure taken from [49].

2.2.2 Charged particles

In contrast to photons, charged particles interact with matter continuously along their path. The detailed nature of this energy loss depends on the mass, charge, and energy of the incident particle.

Light charged particles such as electrons are commonly used in radiotherapy for the treatment of tumors located close to the body surface. Their small mass leads to large angular deflections during collisions, resulting in erratic trajectories. Energy loss occurs predominantly via Coulomb interactions with atomic electrons, which cause ionization and excitation of the medium. Electrons can also interact with atomic nuclei, emitting bremsstrahlung radiation; this process becomes more significant at higher energies and in materials with high atomic numbers [151]. The rate of energy loss (dE), per unit path length (dx) is described by the stopping power S (units of MeV cm^{-1}):

$$S = -\frac{dE}{dx} \quad (2.2)$$

The total stopping power of electrons is given from the contribution of the mechanisms described: $S = S_{col} + S_{rad}$, where S_{col} is the collisional stopping power and S_{rad} is the radiative stopping power. To remove the dependency on the density of the medium, the mass stopping power is often used:

$$\frac{S}{\rho} = -\frac{1}{\rho} \frac{dE}{dx} \quad (2.3)$$

This quantity has units of $\text{MeV cm}^2 \text{g}^{-1}$ and is commonly used to compare energy

loss properties in different materials regardless of density. In therapeutic electron beams with energies up to about 22 MeV, collisional stopping power dominates, and the resulting depth–dose curve falls sharply beyond the therapeutic range as illustrated in Figure 2.2.

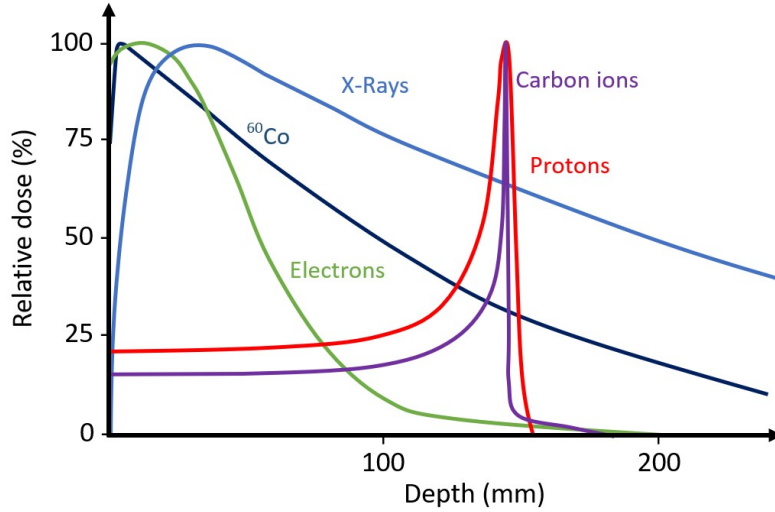


Figure 2.2: Typical percentage depth dose (dose at depth as a percentage of the maximum) distribution for different particles used in radiotherapy.

Heavier charged particles, such as protons and heavy ions, interact with matter similarly to electrons at low energies via Coulomb interactions with atomic electrons. However, due to their greater mass, conservation of momentum implies that they undergo smaller deflections and travel in nearly straight paths through matter [140]. Bremsstrahlung emission is negligible, and at higher energies, additional processes such as scattering from atomic nuclei and non-elastic nuclear interactions may occur, leading to the production of secondary particles.

The interaction of heavy charged particles is described using the mass stopping power, governed by the Bethe-Bloch equation [18], a quantum-relativistic model that predicts the energy loss of heavy charged particles in a medium:

$$-\frac{dE}{dx} = \frac{4\pi k_0^2 Z^2 e^4 n}{m_e c^2 \beta^2} \left[\ln \frac{2m_e c^2 \beta^2}{I(1 - \beta^2)} - \beta^2 - \frac{C}{Z} \right] \quad (2.4)$$

Where k_0 is Coulomb constant, Z atomic number of incident charged heavy particle, e is the electron charge, n the density of electrons in the medium, $m_e c^2$ is electron's mass, $\beta = v/c$ relative speed of the heavy charged particle in relation

to the speed of light, c , I the mean excitation potential of the material and C is the shell correction for low energy effects.

Protons used clinically typically have energies in the range 70–235 MeV, corresponding to ranges in water of approximately 4–32 cm. In this energy range, the stopping power is strongly dependent on the inverse square of the proton's velocity, meaning that the stopping power increases as the particle slows down. This energy regime is especially important because it leads to the characteristic proton dose distribution shown in Figure 2.2. Initially, protons move fast and deposit little energy, resulting in an almost flat dose deposition, the so-called *plateau region* but as they penetrate deeper and lose velocity, the energy deposited per unit length rises sharply, producing the *Bragg peak*, a narrow region of high dose just before the particle comes to rest [180]. It should be noted that for heavier ions the drop in dose after the Bragg peak is less pronounced at the end. This is because these heavy ions undergo nuclear reactions throughout their path, process known as fragmentation, that leads to the formation of ions that are lighter than those in the primary beam which deposit dose beyond the Bragg peak, forming the *fragmentation tail* [101].

The range of heavier charged particles in matter is determined primarily by its initial energy, which makes that protons of different energies come to rest at different depths. A monoenergetic proton beam therefore produces a single, well-defined Bragg peak, which is well suited for targeting a small lesion at a specific depth. However, most clinical tumors extend over a finite volume, making a single Bragg peak insufficient for full coverage. To address this, the incident beam energy is modulated so that multiple Bragg peaks at different depths are superimposed, forming a *Spread-Out Bragg Peak* (SOBP) that conforms to the target volume, as illustrated in Figure 2.3. This dose distribution offers an advantage of particle therapy compared to the conventional radiotherapy: the reduction of the dose to healthy tissue [128] which results in less toxicity which improves patient's quality of life [107], potentially reduces the risk of secondary cancers [139] and allows for other therapeutic options, such as has the possibility of re-irradiate patients with recurring cancers [159]. It should be noted that, in clinical practice, treatment plans typically employ multiple fields, and practical considerations such as range uncertainties, motion, and anatomical changes may reduce the magnitude of the distal-dose sparing advantage, depending on the treatment site and delivery technique.

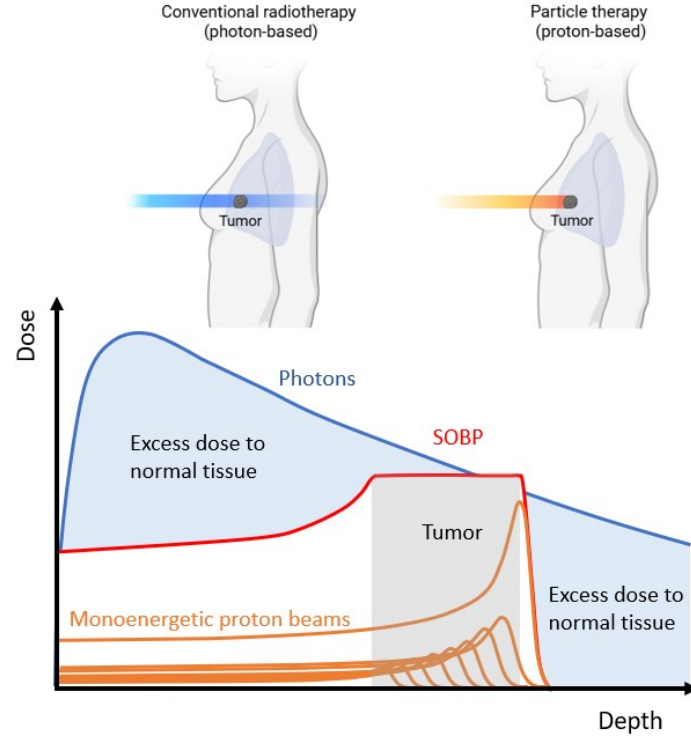


Figure 2.3: Dosimetric differences between conventional radiotherapy based on photons and proton therapy. It can be seen how conventional radiotherapy with a single beam deposits extra dose in the surrounding healthy tissues to achieve the same dose levels as protons at tumor depth. Adapted from [149, 79].

2.3 Quantifying radiation effects

2.3.1 Absorbed Dose

One of the dosimetric quantities that best correlates with the deterministic biological effects produced by ionizing radiation is the absorbed dose¹ [12]. It is a fundamental quantity in radiation physics and dosimetry defined as the mean energy imparted by ionizing radiation ($d\bar{\epsilon}$) to unit mass of matter (dm):

$$D = \frac{d\bar{\epsilon}}{dm} \quad (2.5)$$

Where D is the absorbed dose expressed in units of Grays, equivalent to Joule per kilogram: $1 \text{ Gy} = 1 \text{ J kg}^{-1}$. If the condition of delta-ray particle equilibrium is

¹Although absorbed dose does not correlate with stochastic effects, it remains the relevant quantity for describing deterministic effects, which are the primary focus of radiotherapy.

met, absorbed dose can also be expressed in terms of the fluence of the radiation field [151]. Fluence, denoted by Φ (particles cm^{-2}), is defined as the number of particles incident per unit area. For a monoenergetic beam of particles:

$$D = \Phi \cdot \left(\frac{S_{col}}{\rho} \right) \quad (2.6)$$

Where S_{col}/ρ is the collisional mass stopping power of the medium ($\text{MeV cm}^2 \text{g}^{-1}$). This quantity represents the energy loss per unit path length due to inelastic collisions with atomic electrons, per unit density of the medium, and is directly related to the energy deposited locally. The use of the collision component, rather than the total stopping power, excludes energy losses due to radiative processes, which may result in energy transport out of the local volume.

Alternatively, for non-charged particles, absorbed dose can be written in terms of the energy fluence Ψ (J cm^{-2}) if full charged particle equilibrium is established:

$$D = \Psi \cdot \left(\frac{\mu_{en}}{\rho} \right) \quad (2.7)$$

Where μ_{en}/ρ is the mass energy absorption coefficient ($\text{cm}^2 \text{g}^{-1}$). In radiation dosimetry, this coefficient is preferred over the mass attenuation coefficient μ/ρ , since μ_{en}/ρ quantifies the fraction of photon energy actually absorbed in the medium per unit mass, whereas μ/ρ only describes the attenuation of the photon beam.

2.3.2 Linear Energy Transfer

While stopping power describes the total energy lost by a particle as it moves through a medium, a relevant quantity more directly related to the biological effects of radiation is the Linear Energy Transfer (LET). LET is defined as the average energy deposited locally in the medium per unit path length and is typically expressed in units of $\text{keV } \mu\text{m}^{-1}$ [151].

A portion of the energy lost by the particle may be carried away by secondary particles, particularly δ -electrons that can travel significant distances from the primary particle's path. To account only for the energy deposited near the track, the concept of *restricted LET* (LET_{Δ}) is introduced. LET_{Δ} includes only the energy transferred to secondary electrons with energies below a specified cutoff value Δ . The choice of Δ depends on the spatial resolution or biological scale of interest. LET_{Δ} is therefore a fundamental quantity in radiobiology, as it is closely related to the spatial distribution of energy deposition and its potential to cause complex DNA damage.

If, instead, all of the energy lost to secondary electrons is included, regardless of their energy or range, we arrive at the definition of *unrestricted LET* (LET_{∞}). This quantity is equivalent to the linear collision stopping power [84]. LET_{∞} provides a measure of the total energy loss per unit path length without regard for where the energy is ultimately deposited.

Low-LET radiation, such as photons, produce sparsely distributed ionizations, and are often associated with mainly indirect DNA damage. This sparsely radiation also interacts with other molecules inside the cell, producing chemical reactions that generate free radicals that diffuse and interact with DNA, generating additional damage. Such interactions predominantly result in single-strand breaks or isolated base damage, which can usually be repaired, as the intact complementary DNA strand preserves the information needed to restore the original sequence [151].

As LET increases, so does the density of ionization events along the particle track. High-LET radiation, such as carbon ions, deposits energy densely along its track, producing mainly direct DNA damage, often resulting in complex DNA double-strand breaks, which are difficult for the cell to repair as complementary DNA strand may also be damaged.

2.3.3 Relative Biological Effectiveness

The same absorbed dose, delivered using different radiation qualities, may not yield the same biological effect and the limitations of just using LET become prominent when ions of different atomic number are compared as different biological effects are experimentally observed [174]. The Relative Biological Effectiveness (RBE) was introduced to compare the biological effectiveness of different radiation types. It is defined as the ratio of the absorbed dose required to achieve a specific biological effect using a reference radiation, and the absorbed dose required to produce the same effect using another type of radiation [151]:

$$RBE = \frac{D_{ref}}{D_{test}} \bigg|_{\text{Isoeffect}} \quad (2.8)$$

RBE depends on various factors, including the type of radiation, the biological endpoint, cell type and dose among others. Experimentally, RBE has been found to correlate with the LET value across all types of radiation. At low LET values, RBE remains approximately constant and close to unity. As LET increases, RBE generally rises, reaching a maximum. Beyond this range, further increases in LET result in a decrease in RBE due to the overkill effect, in which energy deposition

becomes excessively concentrated, surpassing the cell's capacity for damage repair [110].

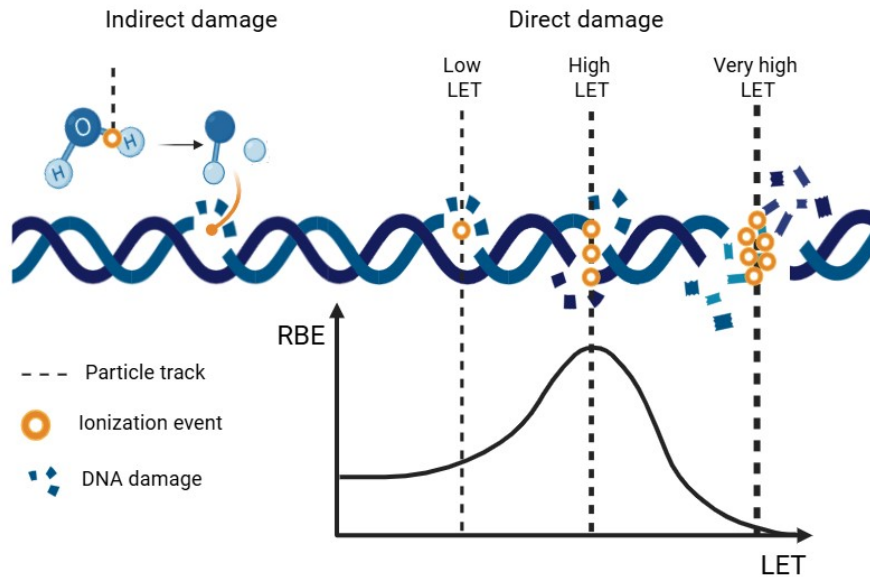


Figure 2.4: Representation of indirect and direct damage to DNA, effects of different LET radiation on DNA strand breaks and relation between LET and RBE. Partially adapted from [55].

In conventional radiotherapy with photon beams, RBE is considered constant. For clinical proton beams, a uniform RBE of 1.1 is generally used. This value is based on historical experimental data and represents a simplification for treatment planning purposes. However, there are indications that RBE for protons is not uniform, and that it increases significantly in the distal dose fall-off the Bragg peak where LET increases. This variability could result in a higher than expected biologically equivalent dose deposition, which can be problematic in normal tissues located distal to the tumor. Carbon ions exhibit RBE greater than 1 across all the range, and also increases with depth. For heavier ions, the RBE maximum is shifted to larger LET values and becomes less pronounced which is not always optimal for radiotherapy purposes as explained in section 2.5.

2.4 Beam technology

2.4.1 Cobalt-60 units

Historically, Cobalt-60 (^{60}Co) units were widely used in external beam radiotherapy. These units continuously emit gamma photons with energies of 1.17 MeV and 1.33 MeV. Radiation is generated through the radioactive decay of ^{60}Co , which is encapsulated and housed within a heavily shielded head. During irradiation, a mechanical system positions the source into an unshielded aperture, where the beam can be directed towards the target field.

Although ^{60}Co units were once the mainstay of external radiotherapy, they have been largely replaced in modern clinical practice by linear accelerators (LINACs). Despite their declining clinical use, ^{60}Co sources remain essential for reference dosimetry. Their stable and well characterized photon spectrum makes them ideal for use as reference radiation beams in the calibration of ionization chambers and dosimetric instruments. As such, they are widely used in primary, secondary standard dosimetry laboratories and national metrology institutes to establish a traceable calibration chain.

2.4.2 LINACs

Linear particle accelerators (LINACs) are widely used in modern external beam radiotherapy and are designed to accelerate low mass charged particles, primarily electrons, to high energies. The process begins in an electron gun, where electrons are generated by thermionic emission from a heated cathode. These electrons are then injected into an accelerating waveguide, where they travel in a straight path and gain energy through interaction with high-power microwaves. After acceleration, a bending magnet system directs the electron beam toward the treatment head. LINACs can operate in either electron mode or photon mode. In photon mode, the accelerated electron beam is directed onto a high atomic number target, typically tungsten, producing bremsstrahlung radiation. Photon energies typically range from 6 MV to 25 MV, allowing for deeper penetration depth.

High dose conformity in advanced techniques such as intensity modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) is achieved through the use of primary, secondary and multi-leaf collimators (MLC), which enable conformal dose distributions tailored to the target volume. This techniques deliver beams from different angles so that each individual beam contributes with a lower entrance dose compared with a single radiation field; when the beams overlap at the tumor site, the doses sum to produce a higher total dose to the target, while lowering the dose to surrounding healthy tissue.

Being inherently pulsed systems, LINACs time structure are best described using the following specific beam parameters according to [24] definitions applicable to any pulsed systems, graphically represented in Figure 2.5:

- Pulse duration (t_{puls}): Time interval between the start of the first bunch to the end of the last bunch in the pulse. A pulse is a basic component of the macrostructure of a beam formed by a train of bunches. A bunch is a basic component of the microstructure of a beam, formed by clusters of particles generated by the electron or ion source. The duration of a single bunch is denoted as t_{bunch} .
- Pulse repetition time (T): The time interval between the start of two consecutive pulses. The pulse repetition frequency, PRF, is defined as the inverse of the pulse repetition time: $PRF = T^{-1}$.
- Total irradiation time (t_{total}): The elapsed time from the start of beam delivery to its completion, including all beam-on and off intervals part of the delivery sequence.
- Total dose (D): Total dose delivered by the beam at a specified reference point or to a reference volume.
- Dose per pulse (DPP): dose delivered within a single pulse. In Figure 2.5 it corresponds to the area of the rectangle, which represents a single pulse.
- Instantaneous dose rate ($\dot{D}_{inst}$): The dose rate during the pulse itself, defined as $\dot{D}_{inst} = DPP / t_{puls}$.
- Average dose rate ($\dot{D}_{av}$): The dose rate averaged over one complete pulse period, defined as $\dot{D}_{av} = D \cdot PRF$. Note that this definition differs from that of the average dose rate over the full irradiation, as it depends significantly on the delivery mode. In particle therapy, for example, the definition on pencil beam scanning (PBS) may differ substantially [47].

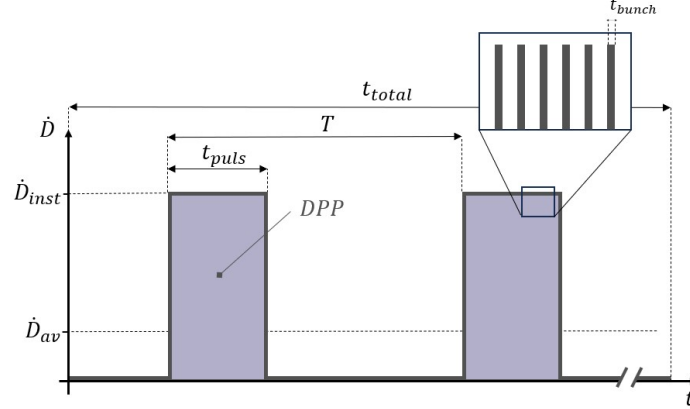


Figure 2.5: Graphical representation of temporal structure of pulsed beam parameters. Adapted from [65].

2.4.3 Accelerators for particle therapy

In particle therapy, circular accelerators are used to accelerate protons and heavy ions to therapeutic energies. Compared to LINACs, they are less widespread due to their greater complexity, cost, and infrastructure demands. Because of this, they are currently in a limited number of specialized centers worldwide [144]. These centers typically use one of these three types of circular accelerators: synchrocyclotrons, isochronous cyclotrons or slow-cycling synchrotrons [129, 192]. Each system uses a different acceleration strategy, which results in different beam characteristics, particularly regarding beam time structure, which is relevant for dosimetry purposes.

All three types use magnetic fields to bend the particle trajectories into circular or spiral paths and apply a RF electric fields to accelerate particles each time they pass between accelerating structure. However, as particles approach relativistic speeds, their effective mass increases, causing them to drift out of phase if a fixed RF frequency is kept. Each system addresses this challenge differently:

Synchrocyclotron

Synchrocyclotrons operate by varying the RF frequency and gradually decreasing the magnetic field during each acceleration cycle to match the changing revolution time of the particles [192]. Because the RF does not vary very quickly, the acceleration is relatively slow and requires many revolutions before extraction. The whole cycle is repeated at a frequency of up to 1 kHz. As a result, it delivers a pulsed beam with a typical pulse duration of 1-10 μ s and a period of 1-3 ms. This

results in a low duty cycle, defined as the fraction of time during which the beam is actively delivered relative to the total cycle, typically ranging 0.1-5%. [129]

Synchrocyclotrons are compact and cost effective accelerators, most commonly employed for single room proton therapy facilities [148, 193, 185]. With the increasing use of proton therapy worldwide, several companies have developed and commercialized compact synchrocyclotron based solutions, such as the IBA S2C2 ProteusONE [81] or the Mevion S250i Hyperscan [122].

Isochronous cyclotrons

Isochronous cyclotrons maintain a constant RF frequency (in the range of 50–100 MHz) by increasing the magnetic field with radius, allowing particles to remain synchronized throughout acceleration. This results in a beam composed of successive 1–2 ns bunches separated by 10–20 ns intervals. Due to the high repetition frequency and regularity of these bunches, the beam appears continuous on clinical or dosimetric timescales, resulting in an effective duty cycle close to 100%.

Typical isochronous cyclotrons are generally larger in size and are often configured to serve multiple treatment rooms [192]. However, superconducting designs have enabled the development of more compact systems [64, 16] thereby reducing overall facility costs. Popular industrial solutions include the IBA 235 ProteusPLUS [82] and the Varian ProBeam 360° [121]. While most existing machines are designed for protons, a new generation of isochronous cyclotrons is being developed to accommodate heavier ions as well [91].

Synchrotrons

Synchrotrons accelerate particles in a circular ring where both the magnetic field and the RF frequency are varied synchronously during the acceleration phase. For clinical use, they operate in slow-cycling mode, delivering spills of particles that follow a regular sequence: injection of particle bunches into the ring, acceleration to the desired energy, slow extraction over multiple turns, and ramp-down. This cycle produces a quasi-continuous beam during extraction phase, with spills typically lasting 1–10 s, spaced by approximately 2 s, and a duty cycle ranging 10-50%. [129, 192]

Synchrotrons are currently used to accelerate protons, as well as heavier ions, including carbon for clinical applications and helium or oxygen for research purposes [190]. Most existing synchrotrons facilities are custom made [35, 42], result of large collaborations with experienced centers. Nevertheless, commercial systems

are also available, such as Hitachi's solutions for protons, heavy ions, and hybrid centers [74, 72, 73].

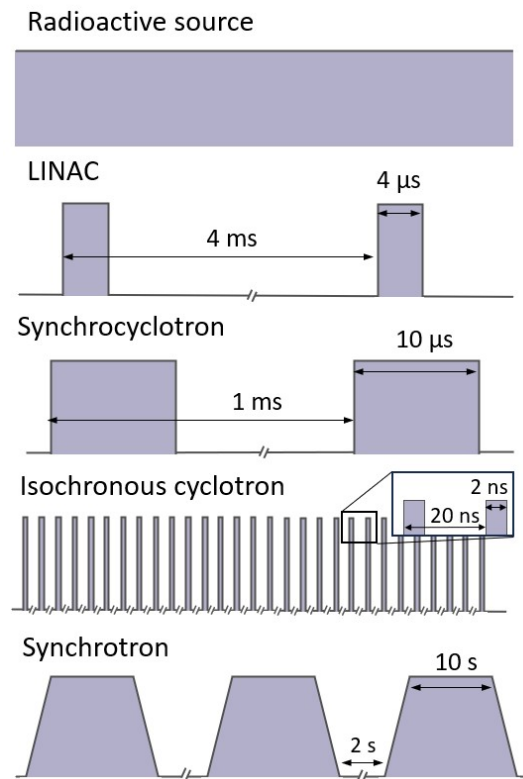


Figure 2.6: Beam time structures of the different beam technologies. Adapted from [170, 52, 157].

Beam transport and delivery

While the type of accelerator determines the initial characteristics of the beam, the subsequent components of particle therapy systems share many similarities across different facilities.

Following the acceleration initial phase, the beam is directed into the beamline, a system of vacuum pipes, magnets, and beam-shaping devices that ensures proper focusing, steering, and energy modulation. Dipole magnets bend the beam's trajectory, quadrupole magnets focus it transversely to maintain the desired size and shape, and steering magnets provide fine positional adjustments. A big distinction between the different accelerator for particle therapy systems is the method based for energy selection, that adds different components into the beamline. Synchro-

clotrons and isochronous cyclotrons produce a beam with fixed maximum energy, therefore they necessitate a energy selection system in the beamline. This system typically includes a carbon wedge degrader, which reduces the particle energy through controlled scattering, followed by dipoles and momentum selection slits that filter out particles with undesirable energy spread. In contrast, synchrotrons are able to vary the extraction energy directly, eliminating the need for degraders and thereby minimizing beam loss and secondary radiation production.

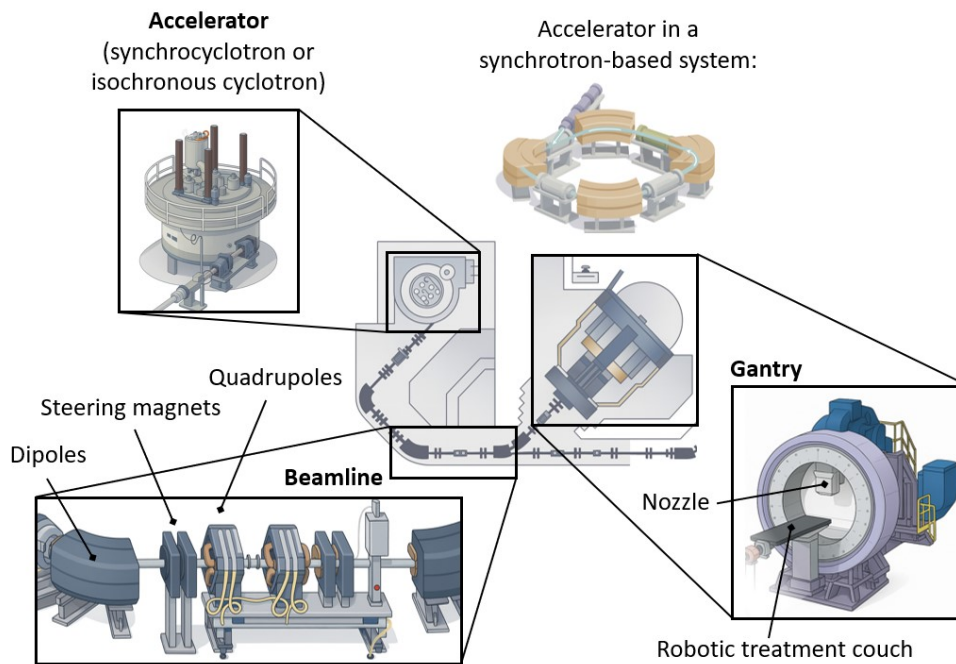


Figure 2.7: Scheme of the different parts of a particle therapy system. Partially adapted from [1, 33].

After beam transport, the particles are delivered to the treatment room via a rotating gantry. This structure allows beam delivery from multiple angles around the patient. At the end of the gantry is the nozzle, which houses the final elements for beam shaping and dose monitoring. These include ionization chambers for real time beam position monitoring and intensity verification, as well as devices to modulate the beam based on the delivery technique employed. Depending on the components of the nozzle, two main beam delivery techniques are recognized: *passive scattering* and *active scanning*.

Historically, *passive scattering* techniques were the first to be widely implemented in clinical proton therapy [140] and are conceptually analogous to conventional X-ray radiotherapy. In this approach, the beam is broadened laterally using scattering foils, and a SOBP is created in depth using range modulators such as ridge filters (for fixed SOBP lengths) or modulator wheels (for variable SOBP widths). This method allows for very rapid dose delivery since the entire SOBP is delivered almost instantaneously. However, it suffers from several drawbacks as it requires the use of patient-specific range compensators and apertures, has poor proximal dose conformity, and generates significant neutron contamination due to beam interactions with the scattering and collimation systems. These limitations have led to a decline in its use.

Active scanning techniques, particularly pencil beam scanning (PBS), are now widely adopted in modern particle therapy centers [117, 32] since their first development [145]. In PBS, the lateral distribution of the dose is achieved by electromagnetically steering narrow proton beams, called spots, across the target volume. Depth modulation is performed by varying the beam energy, delivering a series of iso-energetic layers (energy slices), each corresponding to a specific depth in the tissue. This technique distributes the dose sequentially spot by spot, and layer by layer and provides excellent dose conformity. However, PBS is relatively slow compared to passive methods, primarily due to the energy switching time required between layers, which can be on the order of hundreds of milliseconds.

Figure 2.8 illustrates a representation of the different components and the beam shaping techniques in radiotherapy.

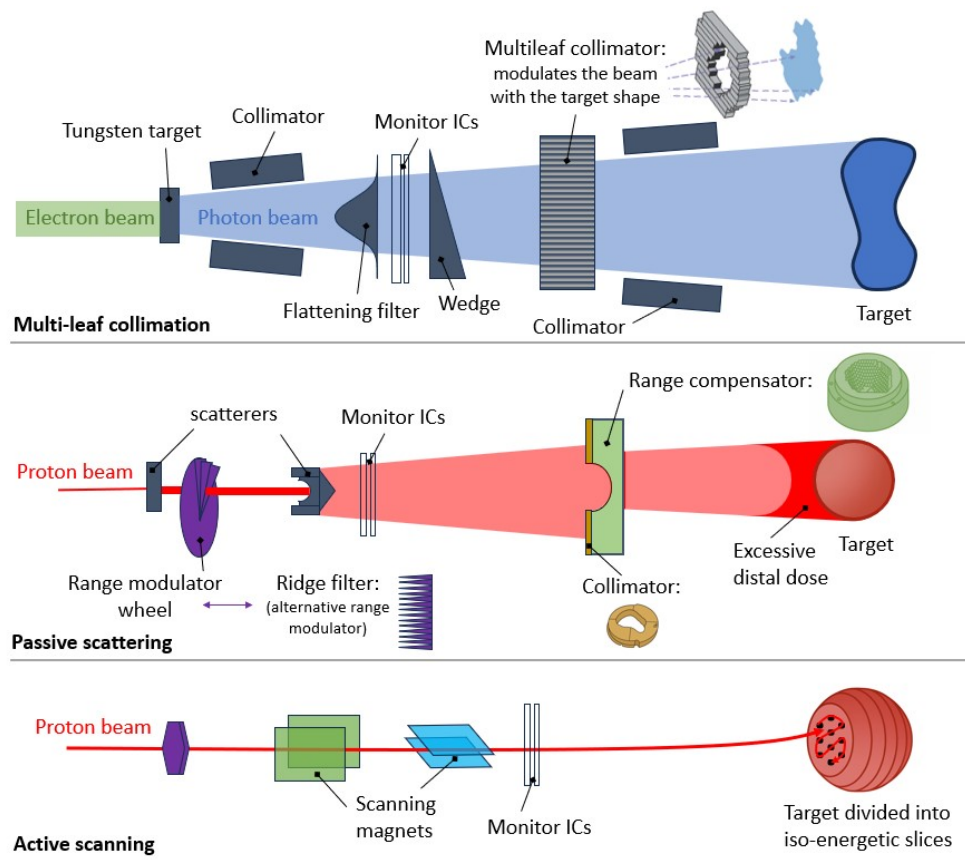


Figure 2.8: Beam shaping in radiotherapy with a LINAC (multileaf system) and particle therapy systems (passive scattering and active scanning). Adapted from [158, 119, 173].

2.5 Rationale and challenges behind novel treatment modalities

2.5.1 High LET particle therapy

A challenge for the effectiveness of cancer treatments remains in certain radioresistant hypoxic tumors. As discussed in previous sections, low-LET radiation such as photons, induces most DNA damage indirectly, via the generation of free radicals. The presence of oxygen enhances this process: oxygen molecules react with the radiation-induced radicals to form stable chemical products that bind to DNA and interfere with repair enzymes, making damage repair more difficult. Many tumors grow rapidly and develop regions of poor vascularization, resulting in varying degrees of hypoxia. Under hypoxic conditions, fewer free radicals are produced, and the DNA damage caused by low-LET radiation is reduced. This means that normoxic healthy tissue can be damaged while the hypoxic tumor remains relatively resistant. Dose escalation can compensate for this loss of tumor control, but it comes at the cost of increased risk to surrounding normal tissues.

High-LET radiation offers a potential solution. Because these particles cause mainly direct ionization of DNA and their effectiveness is much less dependent on oxygen concentration. This makes high-LET beams more effective against hypoxic tumors, delivering comparable damage in both hypoxic and normoxic tissues.

For protons, the RBE remains close to that of photons across most of the beam range, rising significantly only near the distal end of the track where LET increases. In clinical treatments employing a SOBP, this localized RBE increase means that only a small fraction of the tumor volume (Figure 2.9, right) can benefit from the increased RBE.

To achieve consistently higher RBE across the whole tumor volume, heavier ions have been investigated. Oxygen or neon ions have a substantially higher LET; however, they also exhibit increased nuclear fragmentation, producing a broader and more biologically damaging dose tail beyond the target. Moreover, as shown in Figure 2.9 (left), increasing the particle's atomic number reduces the steepness of the LET–RBE relationship, raising the RBE across the full depth–dose curve, including the plateau region. While this may seem advantageous, a high constant RBE across the whole depth–dose curve also increases healthy tissue toxicity. This reduces the therapeutic advantage of high LET particle therapy.

The optimal therapeutic gain occurs when the Bragg peak aligns with the highest RBE, a condition well met by carbon ions. Carbon ions are currently the most

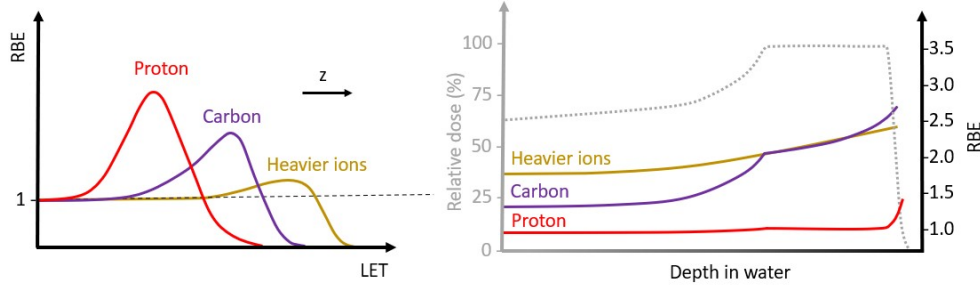


Figure 2.9: Left: Schematic representations of RBE vs LET for different particles with increasing atomic number (Z). Right: Relative dose distribution of an SOBP (dashed grey line) and associated RBEs for different particles (solid colour lines) vs depth in water. Adapted from [100, 189].

widely used heavy ion beam in the clinic because they offer an optimal balance between physical dose distribution and biological effectiveness.

Now a question regarding intermediate ions between protons and carbon may arise, as they could provide an interesting balance between larger RBE than protons and smaller fragmentation tail than carbon ions. In principle, ions such as lithium, beryllium, or boron could be considered. However, their charge to mass ratios ($Z/A \approx 0.43\text{--}0.45$), inversely related to the magnetic rigidity (resistance of a particle to deflection by magnetic fields), make acceleration more challenging [54, 13] as stronger magnets and higher RF are needed for standard clinical synchrotrons, increasing the machine's complexity, size and cost. Carbon ($Z/A \approx 0.5$) can be accelerated efficiently using existing clinical technology. Helium ions ($Z/A \approx 0.5$) have recently attracted attention as a promising alternative [97, 116] as they offer improved lateral dose conformity, a modest RBE increase, and lower nuclear fragmentation compared to carbon, while maintaining simpler beam delivery. Nevertheless, for the treatment of deep-seated and radioresistant tumors, carbon ions remain the most clinically established.

2.5.2 FLASH therapy

Another emerging treatment modality that has gained considerable attention in recent years is FLASH radiotherapy. This technique exploits the recently re-discovered FLASH effect [30, 188, 187]. A biological effect in which preclinical studies have shown that irradiation at ultra-high dose rates ($\dot{D}_{av} \gtrsim 40 \text{ Gy/s}$) can protect normal tissues from radiation induced damage while maintaining tumor control comparable to conventional dose rates ($\dot{D}_{av} \sim 1 \text{ Gy/min}$) [30].

FLASH is one of the most breaking discoveries in recent radiotherapy, however the exact biological mechanism is still not understood. As a result, the precise beam parameters required to trigger the FLASH effect are still under debate. While average dose rates above 40 Gy/s are often cited as a threshold, recent studies give more importance to achieving instantaneous dose rates in the range of 10^4 – 10^9 Gy/s, total irradiation time below 200 ms and fraction doses ≥ 5 Gy [30, 129]. To date, the FLASH effect has been studied most extensively with electron beams, but it has also been observed with X-rays, protons, and, more recently, heavy ions. Significant effort and progress has been made not only in understanding the biology, but also overcoming the technical challenges of beam delivery.

Electron beams have been the most widely studied, since ultra-high dose rates are relatively easy to achieve. Some modern LINACs, typically used for hypofractionated treatments such as intraoperative radiotherapy (IORT), are already capable of delivering average dose rates of several Gy/s and have been modified to reach FLASH compatible dose rates [57, 87]. Other systems, such as clinical LINACs, have been modified by removing the X-ray target to further increase dose rates [108, 124, 43, 154]. By optimizing beam parameters, electron systems can achieve DPP up to 10 Gy, among the highest values studied to date. Nevertheless, electrons are limited by their shallow penetration depth and large lateral penumbra, restricting their use to superficial tumors. Alternatives for deeper targets include very high energy electrons (VHEE), X-rays, or protons. Clinical translation of VHEE (100–200 MeV) or synchrotron generated soft X-rays (< 1 MeV) remains challenging, as no dedicated clinical systems currently exist, even though several facilities are under development [187]. FLASH RT with conventional energy X-rays also remains technically challenging on current photon systems. As described in subsection 2.4.2, X-rays are generated by directing a high-intensity electron beam onto a high atomic number target, where bremsstrahlung photons are produced. This conversion process is intrinsically inefficient, leading to substantial heating of the target. Achieving ultra-high dose rates would require significant higher beam intensities, resulting in thermal loads that are difficult for existing target designs to withstand [17]. This leaves protons the most practical path towards clinical FLASH applications.

For deep-seated tumors, heavy particle beams are therefore the most promising option for rapid clinical translation. Although other particle modalities such as VHEE electrons or advanced photon systems may ultimately challenge this in the longer term. Proton FLASH delivery at ultra-high dose rates has already been demonstrated [53], and early clinical trials using transmission mode are being underway [118, 45]. These approaches, however, involve the use of the plateau

region of protons without modulation, thereby losing the conformality advantage of protons. Even with reduced normal-tissue toxicity due to the FLASH effect, only a 30–50% sparing is expected [129], which may not be acceptable for routine clinical use given the excess dose and toxicity to surrounding normal tissue. Current research is therefore focused on conformal proton FLASH delivery, which remains technically difficult. Energy layer switching with degraders requires at least 100 ms per layer, resulting in total delivery times of around 20 s, too long to observe the FLASH effect. The most viable strategy proposed up to date combines components from passive scattering, such as patient-specific ridge filters and range shifters, with pencil beam scanning, which help to mitigate the mentioned limitation [165, 48].

The accelerator type and associated beam time structure is also important for clinical translation. Isochronous cyclotrons appear to be strong candidates, providing high beam intensity and continuous delivery with average dose rates around 100 Gy/s [129]. Synchrocyclotrons have also been adapted, modifying pulse widths to 20 μ s and repetition rates to 648 Hz, achieving average dose rates up to 200 Gy/s [44]. Modified synchrotrons, capable of fast cycling and extraction within 50 ms, have reached average dose rates of 800 Gy/s, enabling also studies of heavy ion FLASH therapy. FLASH effect has reported to be observed with all this different temporal structures [157], but recent studies on pulsed beams highlight the importance of instantaneous dose rate in the pulse, a definition that does not apply to continuous beams. Further studies are required to establish thresholds and beam parameters for continuous beam time structures.

Challenges remain not only in biology and beam delivery but also in dosimetry. As illustrated in Figure 2.8, many internal beam control systems rely on ionization chambers, which suffer from large ion recombination effects at ultra-high dose rates, complicating not only reference dosimetry, but also real-time beam monitoring. These issues will be further discussed in the following sections.

As closing remarks for the rationale for these novel treatment modalities, both high-LET particle therapy and FLASH radiotherapy independently offer promising strategies for widening the therapeutic window, the dose region that enables tumor control at a doses levels lower than that causing severe toxicity. High-LET beams primarily shift the tumor control probability (TCP) to lower doses, improving effectiveness against radioresistant and hypoxic tumors. At higher beam energies, the reduced RBE also allows for improved sparing of normal tissues, effectively shifting the normal tissue complication probability (NTCP) curve toward higher dose levels. FLASH therapy also shifts the NTCP curve to higher doses through its characteristic biological effect of sparing healthy tissues. While each modality

can independently improve the therapeutic ratio, they also represent complementary strategies that can be used together as illustrated in Figure 2.10. Together, these modalities exemplify the central aim of modern radiotherapy: widening the therapeutic window and maximizing tumor eradication while minimizing normal tissue toxicity [187].

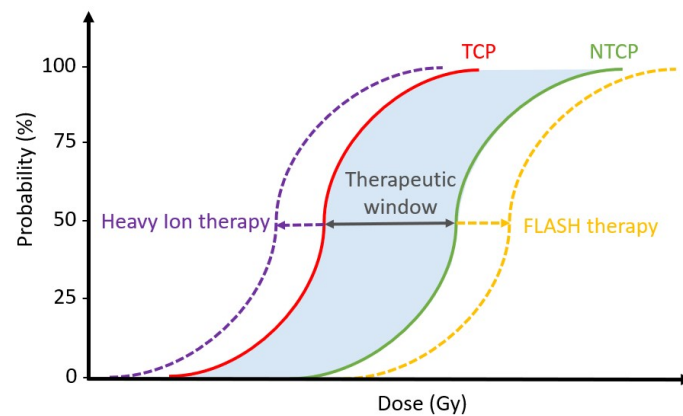


Figure 2.10: Therapeutic window in radiotherapy, represented by the dose region between the sigmoid functions of TCP (red continuous line) and NTCP (green continuous line). Heavy Ion Therapy increases tumor radiosensitivity, shifting the TCP curve to lower doses (purple dashed line) and at higher beam energies with reduced RBE can also improve normal tissue sparing, shifting the NTCP curve to higher doses. FLASH therapy shifts the NTCP curve to higher doses (yellow dashed line). Used separately or in combination, these novel therapies expand the therapeutic window in radiotherapy. Adapted from [187, 166].

2.6 Dosimetry

The therapeutic window in radiotherapy can be very narrow. Since a typical treatment is divided into multiple fractions and only a few Grays are delivered per fraction, a high level of accuracy must be achieved in the delivered dose. According to ICRU Report 24 [85], an accuracy of approximately $\pm 5\%$ in the absorbed dose to the target volume is required for most radiotherapy treatments.

Systematic deviations in the delivered dose can have significant clinical consequences: underdosage may compromise local tumor control and leave the treatment ineffective, while overdosage increases the likelihood of adverse side effects and toxicities associated with radiation. Accurate dose measurement and verification are therefore essential for both patient safety and treatment efficacy.

As discussed in previous sections, radiation beams vary in particle type, energy, modality, and delivery technique. Without standardized procedures, treatment verification would lack consistency across institutions, leading to uncertainties in patient outcomes. Dosimetry provides a solution by establishing reproducible measurement methods that are systematically performed to verify that the planned treatment is delivered precisely. These procedures range from simple, routine daily checks performed before treatments, to more exhaustive and time consuming weekly, monthly, and annual quality assurance tasks. In radiotherapy dosimetry, a wide range of measurements and verifications are performed, however, for external beam radiotherapy, absorbed dose to water remains the primary quantity of interest.

Water is adopted as the reference medium due to its radiological equivalence to soft tissue, widespread availability, and ease of standardization. International dosimetry protocols such as the International Atomic Energy Agency (IAEA) Technical Report Series n.398 (TRS-398) [78] and the American Association of Physicists in Medicine (AAPM) protocol from Task Group 51 (TG-51) [6] establish well defined reference conditions for its determination, ensuring traceability to primary standards laboratories and thereby harmonization of clinical practice worldwide.

A dosimeter can be defined in general terms as any device capable of providing a reading that reflects the average absorbed dose deposited in its sensitive volume by ionizing radiation. A large diversity of detectors are available for the determination of absorbed dose to water: Ionization chambers (ICs), solid-state detectors such as silicon diodes and diamond detectors, passive dosimeters such as thermoluminescent dosimeters (TLDs) and optically stimulated luminescent dosimeters (OSLDs), as well as radiochromic films, alanine dosimeters, and calorimeters, among others. Each detector type has unique advantages and limitations in terms of energy dependence, sensitivity, dose linearity, spatial resolution, and usability.

An ideal dosimeter should be accurate, exhibit linear response with dose, show minimal dependence on dose rate, energy, or beam direction, have high spatial resolution, small physical size, and be convenient to use² [151]. Despite this diversity, ionization chambers remain the most established tool for reference dosimetry in both conventional and particle therapy. Their long standing use is explained by their stability, reproducibility, robustness, well understood response, and the existence of established calibration procedures.

²For example, passive dosimeters do not provide direct readouts. Determining absorbed dose with them requires a separate reading device and often several hours, which makes them less suitable for routine reference dosimetry in the clinic.

2.6.1 Ionization Chambers

According to international reference dosimetry protocols such as IAEA TRS-398 and AAPM TG-51, ionization chambers are the endorsed instruments for the determination of absorbed dose to water. They are gaseous detectors consisting of an air filled cavity, surrounded by water-equivalent materials, and two electrodes connected to an electrometer that applies a potential difference to establish an electric field inside the cavity.

In plane-parallel chambers (PPICs), a guard ring is typically placed near the collecting electrode to minimize edge effects, ensure a uniform electric field and avoid influence of leakage current into the collecting electrode. An illustrative representation of an ionization chamber and its components is shown in Figure 2.11.

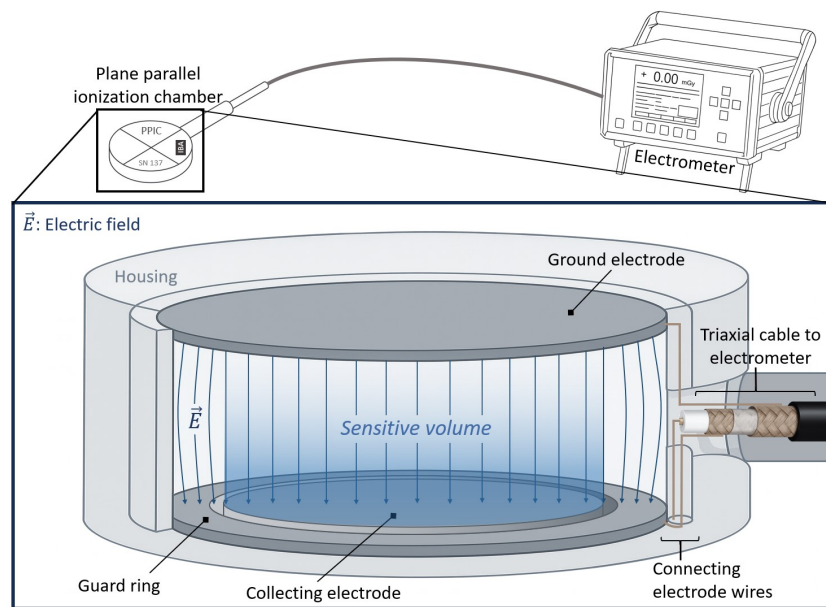


Figure 2.11: Illustration of an ionization chamber connected to an electrometer and schematic representation of the main components of a plane-parallel ionization chamber. Partially adapted from [67].

When an incident radiation particle interacts with the air within the cavity, positive and negative ion pairs are produced. These ions drift under the influence of the applied electric field and are collected at the electrodes. The induced current, which arises due to the movement of charges in the vicinity of the collecting electrode, is measured by the electrometer. The instantaneous current can be

described by the Shockley–Ramo theorem [155]. For the electrode configuration used in ionization chambers, the time integral of this current over the collection period corresponds to the total charge collected at the electrode [75]. In clinical dosimetry, it is this collected charge, rather than the instantaneous current, that is used as the measured quantity.

Although conducting measurements under stable conditions must be always carefully kept, the amount of collected charge is influenced by several external parameters that cannot be controlled and must be corrected for. The most relevant influencing quantities include:

- Air temperature and pressure: The air mass in the sensitive volume of a vented ionization chamber depends on the ambient temperature and pressure, affecting the number of ion pairs produced.
- Humidity: Variations in humidity alter the fraction of water vapor in the air, which can affect parameters such as air density, the mean energy required to produce an ion pair, and the mass stopping power.
- Polarity: The response of an ionization chamber may change depending on the sign of the applied polarizing voltage. A polarity correction accounts for any such variation between the calibration and measurement conditions.
- Ion recombination: Ideally, ionization chambers should operate in the ionization region of gaseous detectors (see Figure 2.12), where all charge carriers created are collected. In practice, this region is very narrow, and partial recombination of ions occurs. Ionization chambers used in radiotherapy therefore require a recombination correction. The different types of recombination, their theoretical basis, and experimental determination will be discussed in detail in the following chapter.
- Charge multiplication: If the electric field is too high, the chamber may begin to operate in the proportional region (see Figure 2.12). In this regime, electrons gain sufficient energy between collisions to cause additional ionizations, leading to a collected charge greater than the initially created ionization. The experimental determination of this correction will also be discussed in later chapters.

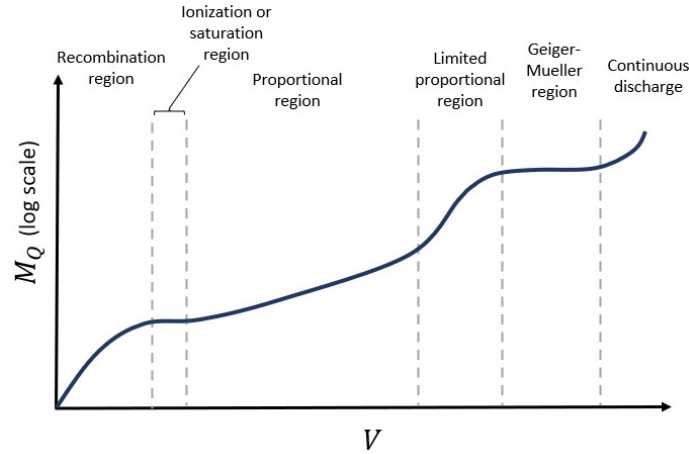


Figure 2.12: Operation regions of gaseous detectors. The collected charge (M_Q , logarithmic scale) is represented as a function of the applied voltage (V). Ionization chambers ideally must operate in the ionization or saturation region, where all charge initially created is collected. Adapted from [131].

Ionization chambers can serve as primary standards provided that the mass of air in the sensitive volume is accurately known. This principle is exemplified by free-air ionization chambers, which are used as primary standards for low-energy x-rays.

However, in practice, ionization chambers are not employed as primary standards for typical radiotherapy beams. Instead, they are used as secondary standards and must be calibrated against a standard traceable to a primary standard to determine a calibration coefficient that relates the collected charge to absorbed dose. This calibration coefficient, N_{D,w,Q_0} , is determined experimentally for each specific chamber in a reference beam quality Q_0 , which is usually a ^{60}Co source. In clinical practice, ionization chambers are used in beam qualities Q that differ from the calibration beam quality. Therefore, a beam quality correction factor, k_{Q,Q_0} , must be applied. Although the first recommendation of TRS-398 is to determine the calibration coefficient directly in the beam quality of use, $N_{D,w,Q}$, in practice, such direct calibrations are rarely feasible as they would require bringing the primary standard to the clinical beam. This is why it is more common to apply generic k_{Q,Q_0} factors for each chamber model. These k_{Q,Q_0} factors are determined through detailed Monte Carlo simulations or experimentally by using a primary standard such as a calorimeter.

According to the TRS-398 formalism, the absorbed dose to water determined with an ionization chamber is obtained through the following expression:

$$D_{w,Q} = M_Q \prod_i k_i \cdot N_{D,w,Q_0} \cdot k_{Q,Q_0} \quad (2.9)$$

where $D_{w,Q}$ is the absorbed dose to water in beam quality Q and M_Q is the charge readout in that same beam quality. To obtain M_Q , the raw measurement is corrected by subtracting the charge measured while the IC is connected to the reading system without being irradiated³. $\prod k_i$ represents the product of the different correction factors associated with the previously explained influencing quantities that affect the chamber reading. These include the polarity correction factor, k_{pol} , that can be obtained as:

$$k_{pol} = \frac{|M_+| + |M_-|}{2|M|} \quad (2.10)$$

where $|M_+|$ and $|M_-|$ are absolute values of the charge readings at positive and negative polarity, respectively, and $|M|$ is the absolute value of the charge reading at the calibration polarity. For most ICs, the polarity correction factor is typically very close to unity. The temperature and pressure correction factor can be determined with the following expression:

$$k_{T,P} = \frac{(273.15 + T)}{(273.15 + T_0)} \frac{P_0}{P} \quad (2.11)$$

where T and P are the ambient temperature and pressure during measurement, respectively, and T_0 and P_0 are the calibration reference conditions (typically $T_0 = 20^\circ\text{C}$ and $P_0 = 1013.25 \text{ hPa}$). Humidity must also be considered: if the calibration coefficient refers to a relative humidity of 50% and the chamber is used within 20–80% RH, no correction is needed, but if calibration in ^{60}Co was performed in dry air, a correction of $k_h = 0.997$ should be applied. Additional corrections include the ion recombination factor k_s , also named the saturation correction factor, and the charge multiplication correction factor k_{CM} . The determination of k_s and k_{CM} is more complex and will be discussed in detail in the following sections. The exact reference measurement conditions for each beam type are detailed in the corresponding codes of practice.

2.6.2 Charge carrier transport dynamics

In the previous section, a general overview of the ionization chamber principle of operation was discussed. In this section, a more detailed explanation of the

³This small signal, typically negligible compared to the signal induced by radiation, originates from surface and volume leakage currents between the polarizing and measuring electrodes or leakage of insulators, cables and electronics.

generation of charge carriers and the different effects they may undergo before collection, with special focus on the recombination process, will be presented.

When an incident radiation particle interacts with an ionization chamber, it ionizes the air contained within its sensitive volume, which is typically composed of approximately 80% nitrogen (N_2) and 20% oxygen (O_2). This ionization produces positive ions (cations) such as N_2^+ and O_2^+ , which act as the primary positive charge carriers. At the same time, electrons (e^-) are released, initially serving as the primary negative charge carriers. However, most of these free electrons undergo a process known as *attachment* (illustrated in Figure 2.13 (c)), in which they combine with neutral molecules of N_2 or O_2 . This process yields anions such as O_2^- and N_2^- , the last one being a non stable ion. After this rapid reaction, the charge carrier population consists mainly of N_2^+ and O_2^+ as positive ions, and O_2^- along with a small fraction of free electrons as negative carriers. This charged species undergo further chemical reactions, leading to the formation of other cations and anions. For clarity, the description is here restricted to the primary ions introduced in this paragraph.

Under the influence of the applied electric field, positive and negative ions *drift* towards the collecting electrode (see Figure 2.13 (a)) at velocities proportional to their mobilities and the electric field. Due to their much larger mass, ion drift is orders of magnitude slower than that of electrons, which are therefore collected almost instantaneously in comparison to the ions. In addition to drift, charge carriers also undergo *diffusion* (Figure 2.13 (b)), migrating towards regions of lower ion concentration. At sufficiently high electric fields, drifting electrons may acquire enough energy to further ionize surrounding ions, leading to *charge multiplication* (Figure 2.13 (e)) and operation in the proportional region of gaseous detectors. Although ionization chambers are designed to avoid this regime, corrections may still be necessary, particularly for chambers with narrow air gaps set at high operating voltages. In certain conditions, such as ultra-high dose rates (UHDR) regimes, the rapid formation of a dense ion population can distort the local electric field through *space charge screening* (Figure 2.13 (f)), thereby reducing the drift velocity of ions.

Recombination events play a crucial role in charge collection efficiency. These involve the neutralization of a positive carrier by a negative one (Figure 2.13 (d)), thereby reducing the total number of charge carriers available for collection and lowering the efficiency of the chamber. Because free electrons are collected rapidly, electron–ion recombination is almost negligible. Instead, most recombination within ionization chambers is dominated by ion–ion processes, mostly through $N_2^+ + O_2^-$ and $O_2^+ + O_2^-$.

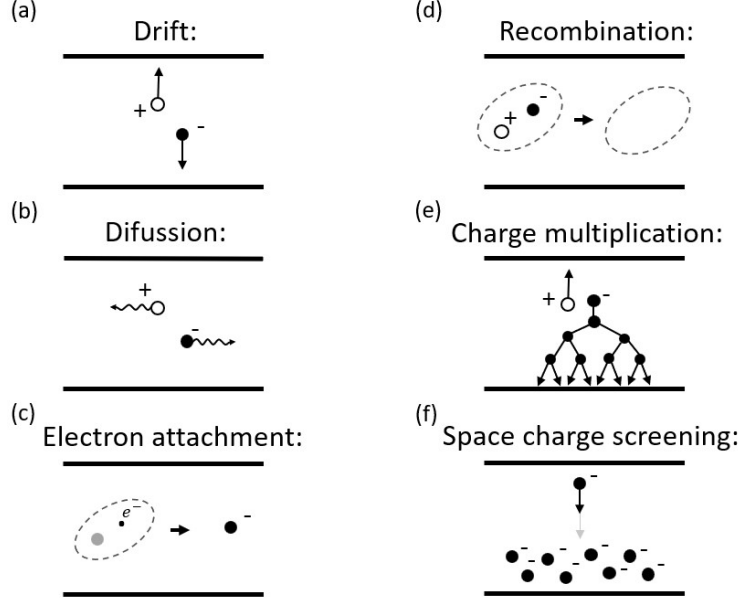


Figure 2.13: Schematic representation of the different processes that charge carriers may undergo during transport. White-filled circles with a nearby “+” symbol represent positive ions (N_2^+ and O_2^+). Black-filled circles with a nearby “-” symbol represent negative ions (O_2^-). Smaller black-filled circles labeled “ e^- ” represent electrons, while grey-filled circles without a symbol correspond to neutral ions (N_2 and O_2).

Recombination is traditionally divided into two types: *initial recombination*, which occurs between ions created by the same incident radiation particle and is strongly related to the LET; and *volume recombination*, which occurs between ions originating from different incident radiation particles and depends primarily on the dose rate. Both types of recombination are illustrated in Figure 2.14.

Depending on the beam time structure, volume recombination is further classified into pulsed or continuous [20]. In dosimetry, the definition of pulsed beam depends on the relation of different beam time parameters in relation with the ionization chamber collection time. This definition is specific to ionization chamber measurements, as the intrinsic classification of the beam should not depend on the detector used. From the ionization chamber perspective, a beam is considered pulsed when the pulse duration (t_{puls}) is much smaller than the collection time of the ionization chamber (τ_{col}), and this is in turn much smaller than the time between pulses (T):

$$t_{puls} \ll \tau_{col} \ll T \quad (2.12)$$

A beam is considered continuous when one or both of these conditions are not satisfied. It is worth noting that typical ionization chamber collection times range from a few tens of microseconds up to about 200 μs [157], depending on the applied voltage and the electrode gap size. The time between pulses is usually long enough to satisfy the second condition for pulsed beams. However, the first condition is more ambiguous: in chambers with small air gaps and high bias voltages, the collection time τ_{col} may approach the order of the pulse duration t_{puls} . In these cases, the assumption of a pulsed beam is not always valid, which leaves the distinction between pulsed and continuous beams somewhat unclear. Reference [132] proposed a practical threshold, suggesting that the boundary between the two regimes occurs when:

$$\frac{t_{\text{puls}}}{\tau_{\text{col}}} \approx 10^{-3} \quad (2.13)$$

However, ionization chambers operating around this intermediate regime remain difficult to categorize, and no theory has yet been formulated to describe this case.

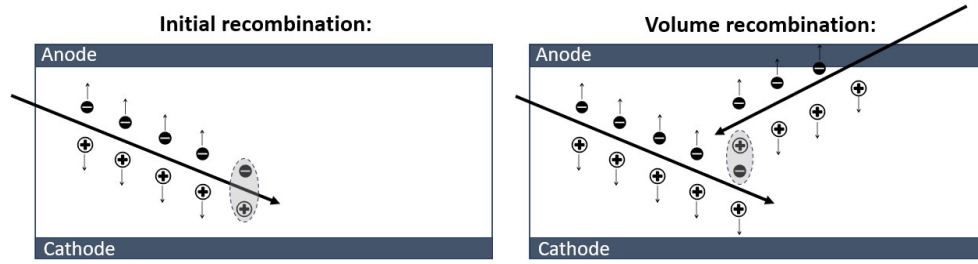


Figure 2.14: Representation of initial recombination (left) and volume, or general, recombination (right).

2.7 Ion recombination theoretical models

The recombination of ions in ionization chambers has been described by several theoretical models. Early work by Onsager [135] focused on the theory of geminate recombination, while Jaffé [88, 94] developed a columnar model that later formed the basis of most treatments of initial recombination. In parallel, Kara-Michailova and Lea [95] extended these ideas by considering recombination within dense clusters of ions. Complementary microdosimetric frameworks introduced amorphous track structure descriptions to represent the spatial distribution of ionization around particle tracks, which is particularly relevant to initial recombination [99, 171, 37]. Volume recombination was first addressed by Mie [123] and subsequently refined in multiple studies [172, 102]. Boag [23, 19] later provided a comprehensive framework to describe recombination in both continuous

and pulsed beams, which remains the standard reference for modern dosimetry protocols.

Although these models are based on different physical assumptions, they try to solve the following non-linear partial differential equation that describes the time evolution of the charge-carrier densities of positive and negative ions ($n_{\pm}$) in a differential volume in the ionization chamber:

$$\frac{\partial n_{\pm}}{\partial t} = D_{\pm} \nabla^2 n_{\pm} \mp \mu_{\pm} \vec{E} \cdot \vec{\nabla} n_{\pm} \mp \mu_{\pm} n_{\pm} \vec{\nabla} \cdot \vec{E} - \alpha n_{+} n_{-}, \quad (2.14)$$

where $D_{\pm}$ is the diffusion constant, $\mu_{\pm}$ the ion mobility, $\vec{E}$ the electric field, and α the recombination constant. The different terms of previous equation correspond, respectively, to effects such as diffusion, drift, space charge screening, and ion recombination.

The following subsections provide a concise description of Jaffé's theory for initial recombination and Boag's formulations for volume recombination, as they are the most widely used models on which experimental methods for determining the ion recombination correction factor with plane-parallel ionization chambers are based. The following overviews are intended to highlight the key assumptions and intermediate steps most relevant for the context of this thesis. Full derivations can be found in the original publications.

2.7.1 Jaffé theory for initial recombination

According to Jaffé's theory for columnar recombination [88, 89], the positive and negative ions created along a track of an incident radiation particle follow a cylindrical distribution with a radial gaussian profile. He approximately solved the previous differential equation 2.14, neglecting terms such as the space charge screening and recombination (since no analytical solution can be found otherwise) to obtain an expression that describes the density of positive or negative ions ($n_{\pm}$) at any given point $r = (x, y, z)$ after a time t :

$$n_{\pm}(r, t) = \frac{N}{\pi(4D_{\pm}t + b^2)} \cdot e^{-\frac{x^2 + y^2 + (z \pm \mu_{\pm} E t)^2}{4D_{\pm}t + b^2}} \quad (2.15)$$

Where N is the linear charge carrier density, b is the initial mean squared radius which experimental studies correlate with LET [163]. At $t = 0$, previous equation effectively means that the distribution of positive and negative ions follow a radial gaussian distribution over a column:

$$n_0(r) = \frac{N_0}{\pi b^2} e^{-\frac{r^2}{b^2}} \quad (2.16)$$

Where N_0 is the initial charge carrier density, given by the ratio between the LET and the mean energy required to form an ion pair ($\bar{w}_{air}$): $N_0 = \frac{LET}{\bar{w}_{air}}$. Jaffé assumed that N decreases over time due to recombination as:

$$\frac{dN(t)}{dt} = -2\pi\alpha \int_0^\infty r n_+(r, t) n_-(r, t) dr \quad (2.17)$$

Substituting expression 2.15 in 2.17, he obtained that:

$$N(t) = \frac{N_0}{1 + \frac{\alpha N_0}{8\pi D_\pm} \ln\left(\frac{4D_\pm t + b^2}{b^2}\right)} \quad (2.18)$$

The ion collection efficiency f (the inverse of k_s) is the ratio between the number of charges collected, $N_{collected}$, and the number of ions created, $N_{created}$. The latter can be calculated as the volume integral of the initial charge distribution from Equation 2.16:

$$N_{created} = \int_0^V n_0(r) dV = N_0 \cdot d \quad (2.19)$$

where d is the distance between electrodes. $N_{collected}$ can be obtained by integrating the number of $2\mu_\pm EN(t)dt$ ions that will escape the overlapping region between positive and negative ions without recombining at a time dt . The time it takes for an ion to be collected is $\tau_{col} \approx d/2\mu_\pm E$, therefore:

$$N_{collected} = \int_{t=0}^{\tau_{col}} 2\mu_\pm EN(t)dt = 2\mu_\pm E \int_{t=0}^{d/2\mu_\pm E} \frac{N_0}{1 + \frac{\alpha N_0}{8\pi D_\pm} \ln\left(\frac{4D_\pm t + b^2}{b^2}\right)} dt \quad (2.20)$$

Finally, f is calculated as:

$$f = \frac{N_{collected}}{N_{created}} = \frac{2\mu_\pm E \int_{t=0}^{d/2\mu_\pm E} \frac{N_0}{1 + \frac{\alpha N_0}{8\pi D_\pm} \ln\left(\frac{4D_\pm t + b^2}{b^2}\right)} dt}{N_0 d} =$$

whose final solution is:

$$f^{ini} = \frac{e^{-1/g}}{gq} [li(e^{1/g + \ln(1+q)}) - li(e^{1/g})] \quad (2.21)$$

where li is the logarithmic integral of the argument ζ , calculated as:

$$li(\zeta) = \int_0^\zeta \frac{1}{\ln(\xi)} d\xi$$

in which ξ is the integration variable and:

$$g = \frac{\alpha N_0}{8\pi D_{\pm}}, \quad q = \frac{2dD_{\pm}}{\mu_{\pm}b^2E} \quad (2.22)$$

This expression is valid only when initial recombination is present and the tracks created are parallel to the electric field.

2.7.2 Boag theory for volume recombination in pulsed beams

Boag's original model

In this first theory [19], Boag formulated a model under two main assumptions, along with neglecting charge screening and diffusion, that allow to simplify the problem. The first assumption is that the ions created initially are homogeneously distributed within the chamber volume. The second is that all electrons created in the initial ionization event attach to neutral ions to form negative ions. In the region where negative and positive ions overlap, the density of ions is diminished equally and constantly due to recombination losses as:⁴

$$\frac{dn_{\pm}}{dt} = -\alpha n_+ n_- \approx -\alpha n^2 \quad (2.23)$$

At a certain time t , the density of ions is:

$$dn = \int -\alpha n^2 dt \quad \rightarrow \quad n(t) = \frac{n_0}{1 + \alpha n_0 t} \quad (2.24)$$

Where n_0 is the initial ion density. The positive and negative ions drift with a constant speed $\vec{v}_{\pm} = \mu_{\pm} \vec{E}$, and the overlapping region between positive and negative ions decreases over the collection time as $\tau_{col} \approx d/(v_+ + v_-)$. It can be deduced that the total number of ions per unit area that escape from the overlapping region in a time interval dt is $n(t)(v_+ + v_-)dt$. Similarly as in Jaffé's theory, f is the ratio between the number of charges collected and the number of ions created. Equally, $N_{created} = n_0 \cdot d$ and $N_{collected}$ can be calculated as the integral of the rate of ions that will escape the overlapping region between positive and negative ions without recombining at a time dt :

$$N_{collected} = \int_{t=0}^{\tau_{col}} n(t)(v_+ + v_-)dt \quad (2.25)$$

⁴Note on notation: due to this assumptions, from now on the notation for the density of ions is reduced to simply n .

The ion collection efficiency is then:

$$f = \frac{N_{collected}}{N_{created}} = \frac{\int_{t=0}^{d^2/(\mu_+ + \mu_-)V} \frac{n_0}{1 + \alpha n_0 t} (\mu_+ + \mu_-) \frac{V}{d} dt}{n_0 \cdot t} \quad (2.26)$$

after solving it we arrive to the solution:

$$f_0^{vol,pulsed} = \frac{1}{u} \ln(1 + u) \quad (2.27)$$

with

$$u = \frac{\alpha n_0 d^2}{(\mu_+ + \mu_-)V} \quad (2.28)$$

where the different constants have already been defined previously.

Accounting for the free electron fraction

As described in section 2.6.2, electrons produced in the initial ionization typically attach to neutral molecules to form negative ions. However, in ionization chambers operated at high voltage or with a small electrode gap, the electric field can be sufficiently large that a fraction of electrons do not attach and are rapidly collected as free electrons. This reduces the negative ion concentration and increases the charge collection efficiency.

The *free electron fraction* (FEF), denoted numerically as p , was incorporated by Boag in his pulsed beam theory [22]. He proposed the fraction of electrons created within a pulse that cross a gap d without attachment as:

$$p = \frac{v_e \gamma}{d} (1 - e^{-\frac{d}{v_e \gamma}}) \quad (2.29)$$

Where v_e is the drift velocity of free electrons and γ is the mean electron lifetime.

Consistent with this definition, the concentration of negative ions changes with the distance z from the negative electrode as:

$$n_-(z) = n_0 (1 - e^{-\frac{z}{v_e \gamma}}) \quad (2.30)$$

Including this spatial distribution of negative ions into the transport equation 2.14 (even with the simplifying assumptions used in the original model) does not yield an analytical solution. Boag therefore introduced three approximations of the distribution of negative ions (visually represented in Figure 2.15) which lead to three different models that account for FEF in pulsed beams:

- Model I: Assumes that the initial negative ion density is uniformly reduced by $(1 - p)n_0$ throughout the gap.
- Model II: Assumes that there is a depletion layer of width pd adjacent to the negative electrode formed by only free electrons. In the remaining region of width $(1 - p)d$ the negative ion density equals the positive ion density.
- Model III: Assumes that the negative ion density is reduced to $(1 - \lambda)n$ uniformly over a region of width $(1 - \lambda)d$, while free electrons are distributed between 0 and λd , where $\lambda = 1 - \sqrt{1 - p}$.

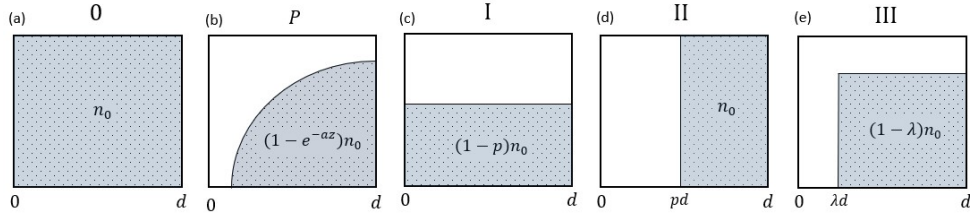


Figure 2.15: Representation of negative ion distribution according to Boag original model 0 (a), proposed distribution of FEF according to Equation 2.30 (b), and approximated distributions of from Boag models models I, II and II corresponding to (c), (d) and (e), respectively. The plots represent a 50% free electron fraction, $p = 0.5$. Adapted from [22].

Boag's Model I

Starting with model I, following the same assumptions as in the original model, but with the reduction of the negative ion density to $(n - pn_0)$, Equation 2.23 is:

$$\frac{dn_{\pm}}{dt} \approx -\alpha n(n - pn_0) \quad (2.31)$$

At a certain time t the density of ions is then:

$$n(t) = \frac{pn_0}{1 - (1 - p)e^{-\alpha n_0 p t}} \quad (2.32)$$

Following a similar derivation as previous model, the integral of the rate of ions that escape the overlapping region is:

$$N_{collected} = \int_{t=0}^{\tau_{col}} n(t)(\mu_+ + \mu_-) \frac{V}{d} dt \quad (2.33)$$

by changing variables $w = e^{-\alpha n_0 p t}$ and $u = \frac{\alpha n_0 d^2}{(\mu_+ + \mu_-)V}$ and substituting on previous equation, we arrive to:

$$N_{collected} = \int_1^{e^{-(1-p)w}} -\frac{dw}{w(1-(1-p)w)} = \frac{n_0 d}{u} \ln\left(1 + \frac{1}{p}(e^{pu} - 1)\right) \quad (2.34)$$

The expression for ion collection efficiency in Boag's model I for pulsed beams, including his first approximation of the distribution of free electrons is then:

$$f_I^{vol,pulsed} = \frac{1}{u} \ln\left(1 + \frac{e^{pu}-1}{p}\right) \quad (2.35)$$

where the different parameters have been previously defined.

Boag's Model II

Derivation of Model II is the same as the original model, but the collection time, taking into account that in this model negative ions occupy the remaining space $((1-p)d)$ that the layer of electrons of width pd do not occupy, becomes:

$$\tau_{col} = \frac{pd}{(\mu_+ + \mu_-)V} \quad (2.36)$$

and the number of ions collected is calculated from a similar integral to 2.25, with the limit of collection time given in eq. 2.42, and previous definition of u :

$$N_{collected} = \int_{t=0}^{\frac{pd^2}{(\mu_+ + \mu_-)V}} \frac{n_0}{1 + \alpha n_0 t} \frac{V}{d} (\mu_+ + \mu_-) dt = n_0 d \frac{1}{u} \ln(1 + (1-p)u) \quad (2.37)$$

The expression for ion collection efficiency in Boag's model II for pulsed beams, including a second approximation of the distribution of free electrons is then:

$$f_{II}^{vol,pulsed} = p + \frac{1}{u} \ln(1 + (1-p)u) \quad (2.38)$$

with the different parameters previously defined.

Boag's Model III

Lastly, for model III, both the density of negative ions and its distribution differ. It assumes that the negative ion density is reduced as $(1-\lambda)n$, homogeneously distributed in a layer of width $(1-\lambda)d$. The total negative charge remaining after clearance of free electrons is $n_0 e (1-\lambda)^2 d$, which must be equal to $(1-p)n_0 e d$, since $p n_0 e d$ is the charge transported by electrons. Therefore:

$$(1-p) = (1-\lambda)^2 \rightarrow \lambda = 1 - \sqrt{(1-p)} \quad (2.39)$$

Similar as done in previous models, Equation 2.23 becomes:

$$\frac{dn_{\pm}}{dt} \approx -\alpha n(n - \lambda n_0) \quad (2.40)$$

leading to the density of ions at a certain time t :

$$n(t) = \frac{\lambda n_0}{1 - (1 - \lambda)e^{-\alpha n_0 \lambda t}} \quad (2.41)$$

and collection time:

$$\tau_{col} = \frac{(1 - \lambda)d^2}{(\mu_+ + \mu_-)V} \quad (2.42)$$

The integral of the rate of ions that escape the overlapping region for this model from Equation 2.33, changing the variables:

$$w = e^{-\alpha n_0 \lambda t} \quad \text{and} \quad u = \frac{\alpha n_0 d^2}{(\mu_+ + \mu_-)V} \quad (2.43)$$

The number of ions collected is:

$$N_{collected} = \int_1^{e^{-\lambda(1-\lambda)u}} -\frac{dw}{w(1 - (1 - \lambda)w)} = \frac{n_0 d}{u} \ln\left(1 + \frac{1}{\lambda}(e^{\lambda(1-\lambda)u} - 1)\right) \quad (2.44)$$

The expression for ion collection efficiency in Boag's model III for pulsed beams, including his third approximation of the distribution of free electrons is then:

$$f_{III}^{vol,pulsed} = \lambda + \frac{1}{u} \ln\left(1 + \frac{1}{\lambda}(e^{\lambda(1-\lambda)u} - 1)\right) \quad (2.45)$$

The three modified versions of the original model predict lower recombination than the original model, as lower number of negative ions are available to recombine, typically:

$$f_0^{vol,pulsed} < f_I^{vol,pulsed} < f_{III}^{vol,pulsed} < f_{II}^{vol,pulsed}$$

2.7.3 Boag theory for volume recombination in continuous beams

Boag's theory dedicated to continuous beams [23], assumes again homogeneous distribution of ions and neglected diffusion and space charge screening contributions, leaving Equation 2.14 for positive ions with simplified notation from previous section as:

$$q = -\frac{d}{dx}(v_+ n_+) - \alpha n_+ n_- \quad (2.46)$$

Where q is the ionization intensity (in $\text{C cm}^{-3} \text{ s}^{-1}$) in steady state. The ionization current density $\bar{q}$ (units of $\text{C cm}^{-2} \text{ s}^{-1}$) is defined as:

$$\bar{q} = n_+ v_+ + n_- v_- \quad (2.47)$$

An approximated expression can be obtained from the assumption that the density of positive ions rises linearly from zero to a maximum value at the negative electrode, and the opposite for negative ions. So that the density of positive and negative ions at a distance x from the positive electrode are:

$$\begin{aligned} n_+(x) &= \left(1 - \frac{x}{d}\right) \frac{fqd^2}{\mu_+V} \\ n_-(x) &= \frac{x}{d} \frac{fqd^2}{\mu_-V} \end{aligned} \quad (2.48)$$

Defining the average rate of recombination R and substituting expressions from Equations 2.48 we obtain:

$$R = \frac{1}{d} \int_0^d \alpha n_+(x) n_-(x) dx = \frac{\alpha f^2 q^2 d^4}{6\mu_+\mu_-V^2} \quad (2.49)$$

If the fraction of total charge liberated per unit of volume destroyed by recombination is $1 - f$, so that:

$$R = (1 - f)q \quad (2.50)$$

Rewriting Equation 2.50 as $f = 1 - R/q$ and substituting Equation 2.49 we arrive to a quadratic expression of f , whose positive root is Boag's expression of the collection efficiency for volume recombination in continuous beams:

$$f^{vol,cont} = \frac{2}{1 + \sqrt{1 + \frac{2}{3}\xi^2}} \quad (2.51)$$

where:

$$\xi^2 = \frac{\alpha d^4 \bar{q}}{\mu_+\mu_-V^2} \quad (2.52)$$

in which the different parameters have been defined previously.

2.8 Experimental methods in non-saturation regime

In the following subsection, the most established experimental methods endorsed in TRS-398 will be presented and discussed. TRS-398 recommends that the ion recombination correction factor for ionization chambers be determined experimentally.

The main reason is to avoid dealing directly with complex theoretical expressions that heavily depend on the parametrization of different constants and instead obtain k_s in a more practical manner. This is achieved by developing simplified

expressions based on a first-order Taylor series expansion, where only one constant needs to be experimentally determined. As a result, linear relationships can be established that are easier to apply in practice.

Traditionally, TRS-398 has recommended the *two-voltage method* (2VM) as the standard approach. However, with the increasing number of centers using particle therapy, this method shows certain limitations. For continuous beams, the 2VM is applicable only when initial recombination is negligible; otherwise, it leads to an underestimation of the ion recombination [68].

In the recent update of TRS-398, new recommendations based on the study of *Jaffé plots* (inverse of the charge collected versus inverse of the applied voltage) have been introduced to address these situations. Both the traditional two-voltage method and the newly endorsed approaches will be described in the following subsections.

Before introducing these methods, it is useful to recall the description of chamber behavior through the *saturation curve*, a plot of the chamber response (current I or collected charge M) as a function of the applied voltage V determined under the same irradiation conditions that is helpful to identify the different regions of an ionization chamber. The collection efficiency is defined as the ratio:

$$f = \frac{M}{M_{sat}} \quad (2.53)$$

or alternatively I/I_{sat} , where M_{sat} and I_{sat} are the saturation values of M and I , respectively. The relationship between M and M_{sat} can also be expressed as the reciprocal of the collection efficiency, which is the ion recombination correction factor:

$$k_s = \frac{M_{sat}}{M} \quad (2.54)$$

As illustrated in left panel of Figure 2.16, in the saturation region, $f = 1$ and $k_s = 1$. In the near-saturation regime when recombination losses are present, $f < 1$ and $k_s > 1$. In contrast, in the proportional region $f > 1$, and k_s is no longer meaningful. In this case, the inverse of the collection efficiency corresponds instead to the charge multiplication correction factor, $k_{CM} < 1$. In some chambers with a very small air gap, the saturation region is extremely narrow, so that both recombination and charge multiplication regions coexist.

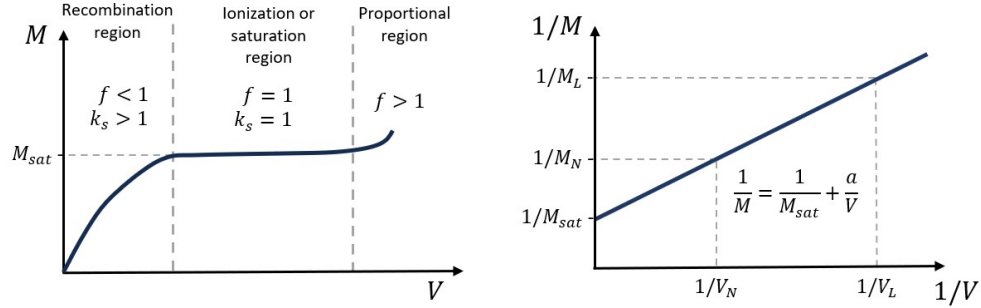


Figure 2.16: Left: Typical saturation curve for an ionization chamber, where M_{sat} is the saturation charge. Right: Jaffé plot ($1/M$ vs $1/V$) on the recombination region where a linear extrapolation to determine M_{sat} , inverse of two voltages ($1/V_N$ and $1/V_L$) and its corresponding inverse of charge measured ($1/M_N$ and $1/M_L$) for the two voltage method in pulsed beams is represented.

2.8.1 Two Voltage Method

In the IAEA TRS-398 Code of Practice, the two-voltage method (2VM) is the endorsed approach to experimentally determine the ion recombination correction factor k_s [78]. Different expressions are used depending on the beam type (pulsed or continuous) and the magnitude of the recombination correction.

Pulsed beams

In the near-saturation region, a first-order Taylor series expansion around $1/V = 0$ of Boag's expression for pulsed beams (Equation 2.27) simplifies k_s , or the inverse of the collection efficiency to:

$$k_s \simeq 1 + \frac{a}{V} \quad (2.55)$$

where a is a constant that should be determined for each particular chamber and irradiation conditions, whose theoretical value is $a = \frac{\alpha \bar{q} d^2}{e \mu}$. Combining with Equation 2.54 we obtain:

$$\frac{1}{M} = \frac{1}{M_{sat}} + \frac{a}{V} \quad (2.56)$$

so that plotting $1/M$ versus $1/V$ yields a straight line. Extrapolation to $1/V = 0$ gives $1/M_{sat}$ as illustrated on Figure 2.16.

The idea behind this method is that the correction can be derived from measurements under the same irradiation conditions at two polarizing potentials: The chamber signal M_N is measured at the nominal operating voltage V_N , and M_L is

the charge collected at a lower voltage V_L . Equation 2.56 can be written for both cases as:

$$\frac{1}{M_{sat}} = \frac{1}{M_N} - \frac{a}{V_N} = \frac{1}{M_L} - \frac{a}{V_L} \quad (2.57)$$

From this relation, the constant a can be expressed as:

$$a = \frac{\frac{1}{M_N} - \frac{1}{M_L}}{\frac{1}{V_N} - \frac{1}{V_L}} = \frac{\frac{V_N}{M_N}(1 - \frac{M_N}{M_L})}{1 - \frac{V_N}{V_L}} \quad (2.58)$$

By substituting Equation 2.58 into the left-hand equality of Equation 2.57 and then into Equation 2.54, the ion recombination correction factor at the nominal voltage V_N can be obtained as:

$$k_s = \frac{n - 1}{n - (M_N/M_L)} \quad (2.59)$$

where $n = V_N/V_L$. TRS-398 specifies that this previous expression should be used if $k_s < 1.03$. Otherwise, assuming linearity between $1/V$ and $1/M$, the protocol recommends using the following quadratic polynomial expression:

$$k_s = a_0 + a_1 \left(\frac{M_N}{M_L} \right) + a_2 \left(\frac{M_N}{M_L} \right)^2 \quad (2.60)$$

where the coefficients a_i are tabulated in TRS-398 for pulsed and pulsed-scanned beams.

It is worth noting that TRS-398 does not include the free electron fraction, as it assumes that its effect is negligible for conventional modalities and PPICs operated at relatively low electric fields. More recent work [106] has introduced expressions that include this effect for the two-voltage method. However, these corrections are not commonly applied in practice, since they depend on constants that vary considerably on the experimental conditions and are not well established.

Continuous beams

In the near-saturation region a first-order Taylor series expansion around $1/V = 0$ of Boag's theory for continuous beams in Equation 2.51 leads to the following polynomial approximation for the collection efficiency:

$$k_s \approx 1 + \frac{b}{V^2} \quad (2.61)$$

where b is a constant dependent on each particular chamber and irradiation conditions, whose theoretical value is $b = \frac{\alpha \bar{q} d^4}{e \mu^2}$.

Following the same derivation as for pulsed beams, the expression for the recombination correction factor at the nominal voltage V_N in the case of a continuous beam is:

$$k_s = \frac{n^2 - 1}{n^2 - (M_N/M_L)} \quad (2.62)$$

where $n = V_N/V_L$.

In TRS-398 it is mentioned that volume recombination on continuous beams can occur in ^{60}Co beams or in kilovoltage X-rays, where the radiation field is clearly continuous. However, the protocol also notes that in these cases the dose rate is usually so low that the contribution of volume recombination is almost negligible, and therefore nearly all recombination is attributed to initial recombination. A similar situation may occur for quasi-continuous proton beams at low dose rates, where initial recombination is expected to dominate.

Contribution of initial recombination

Using a first-order Taylor series approximation of Jaffé's expression for initial recombination around $1/V = 0$, the inverse of Equation 2.21, k_s , can be simplified and approximated as:

$$k_s \simeq 1 + \frac{a'}{V} \quad (2.63)$$

where a' is a constant whose theoretical value is $a' = \frac{qDd^2}{\mu b^2}$, with the parameters defined in Equations 5.10 or in Section 2.7.1. Following a derivation similar to the pulsed case, one arrives at the same experimental expression obtained for pulsed beams, meaning that initial recombination can be determined experimentally using Equation 2.59 from the pulsed beam case.

There are also situations where initial recombination coexists with volume recombination, and both contribute simultaneously. In this case, the total ion recombination correction factor is written as

$$k_s^{total} = k_s^{ini} \cdot k_s^{vol} \quad (2.64)$$

where k_s^{ini} is the contribution from initial recombination and k_s^{vol} is the contribution from volume recombination (either pulsed or continuous).

If initial and volume recombination coexist for continuous beams, the assumed linearity between $1/M$ and $1/V$ (or $1/V^2$) is no longer valid. In this situation, the previous two-voltage method expressions cannot be directly applied. To address this, De Almeida and Niatel [130] proposed an experimental approach based on the two-voltage method applied at different dose rates. The method consists of

performing measurements at two polarizing voltages, V and V/n , for various dose rates. From the ratio of ionization readings at these two voltages, the parameters describing initial and volume recombination, A and B , can be obtained by fitting the following relation to the data:

$$\frac{M_V}{M_{N/n}} = 1 + (n-1)\frac{A}{V} + (n^2-1)\frac{B}{V^2}M_V \quad (2.65)$$

The combined experimental expression for k_s at the operating voltage V_N is then:

$$k_s^{total} = 1 + \frac{A}{V_N} + \frac{B}{V_N^2}M_N \quad (2.66)$$

In the case of pulsed beams, the second term of this previous expression 2.66 becomes $(n-1)\frac{B'}{V}M_V$, where only a linear dependence is observed [142]. The corresponding combined expression for k_s at the operating voltage V_N is:

$$k_s^{total} = 1 + \frac{A}{V_N} + \frac{B'}{V_N}M_N \quad (2.67)$$

2.8.2 Charge multiplication correction

As shown in Figure 2.16, when the polarizing voltage is increased sufficiently, an ionization chamber may enter the proportional region of operation, where charge multiplication occurs. The charge multiplication correction factor follows a negative exponential dependence on the applied voltage V :

$$k_{CM} = e^{-\gamma V}, \quad (2.68)$$

where γ is a geometrical parameter. Although it has not been extensively studied, result from [164, 141] indicate that this parameter depends mainly on the chamber geometry, in particular the air volume or gap thickness, and appears to be independent of beam quality. To determine this factor experimentally, the chamber can be used in a beam where recombination losses are negligible, or, if present, corrected for. By obtaining a full Jaffé plot, the value of γ can then be extracted from a fit to the exponential expression 2.68.

In practice, if the voltage used by the customer is the same as the voltage used for the calibration this correction is normally included in the calibration factor of the ionization chamber and therefore should not be applied again when determining absorbed dose to water. However, charge multiplication disturbs the linearity assumption required for the two-voltage method. To minimize this effect, it is recommended that the ratio of applied voltages, n , remain within a moderate range (typically $2 \leq n \leq 5$) in order to avoid operating at excessively high voltages [151].

It is generally not recommended to operate ionization chambers in the proportional region due to the risk of electrical breakdown of insulators and the additional uncertainties introduced. Nevertheless, in practice many modern ionization chamber designs often reduce the air-gap size to limit recombination losses⁵ which may become substantial in some beam modalities (commercial chambers such as the Advanced Markus chamber from PTW has 1 mm gap [2], while the PPC05 from IBA has 0.6 mm [3]). While this approach reduces recombination, it also increases the likelihood of operating near the proportional region, making charge multiplication corrections more relevant than in conventional parallel-plate ionization chambers with a 2 mm gap (e.g., the PPC40 from IBA [4] or the Roos chamber from PTW [5]).

A comprehensive discussion of experimental scenarios and recommendations on the use of this correction factor is provided in [164]. The following subsection will address in more detail how to correct for recombination when charge multiplication is present.

2.8.3 Jaffé Plot Method

The two-voltage method relies on the assumption of an approximately uniform charge carrier distribution, which is generally valid for photon and electron beams. However, its applicability to light ion beams is questionable [142, 163]. Several factors contribute to this limitation: the classification of particle beams as either continuous or pulsed with respect to ion recombination is not always straightforward, making it difficult to verify linear regions using only two voltages; recombination losses can be significantly large; and under certain conditions, charge multiplication may also occur, leading to the coexistence of recombination and multiplication effects.

In high-energy particle beams, isochronous cyclotrons and synchrotrons generally behave as continuous beams with respect to recombination [162], while synchrocyclotrons deliver short pulses separated by relatively long intervals, behaving as pulsed beams [163]. At high polarizing voltages, the pulse duration may be comparable to the ion collection time. To determine whether a beam behaves as continuous or pulsed with respect to recombination, a Jaffé plot ($1/M$, versus $1/V$) should be constructed under the conditions of interest. If a linear relationship between $1/M$ and $1/V$ is observed, the beam is considered pulsed. In contrast, a quadratic dependence between $1/M$ and $1/V$, or a linear dependence between $1/M$ and $1/V^2$, indicates continuous-beam behavior. If the expected

⁵In all theoretical descriptions of ion recombination the probability of recombination increases with the electrode spacing and decreases with the strength of the electric field.

trends are confirmed at conventional dose rates, the same models proposed in the 2VM can be applied [111, 163]. Examples of the differences in Jaffé plots for each case are illustrated in Figure 2.17.

For higher-LET beams, both initial and volume recombination may be present, and their relative dominance depends on the applied voltage, typically exhibiting an inflection point: at high voltages, initial recombination dominates, whereas at low voltages, the collection efficiency is mainly affected by volume recombination [163]. To evaluate each contribution, the use of De Almeida method is recommended, and it has been shown to be valid for particle beams [142]. If initial recombination is dominant, a linear relationship between $1/M$ and $1/V$ may be observed. In some cases, however, this approximation may not be fully adequately describe the data [162]. In such situations, the full Jaffé theory, which predicts a logarithmic dependence (see Figure 2.17), provides a more accurate description.

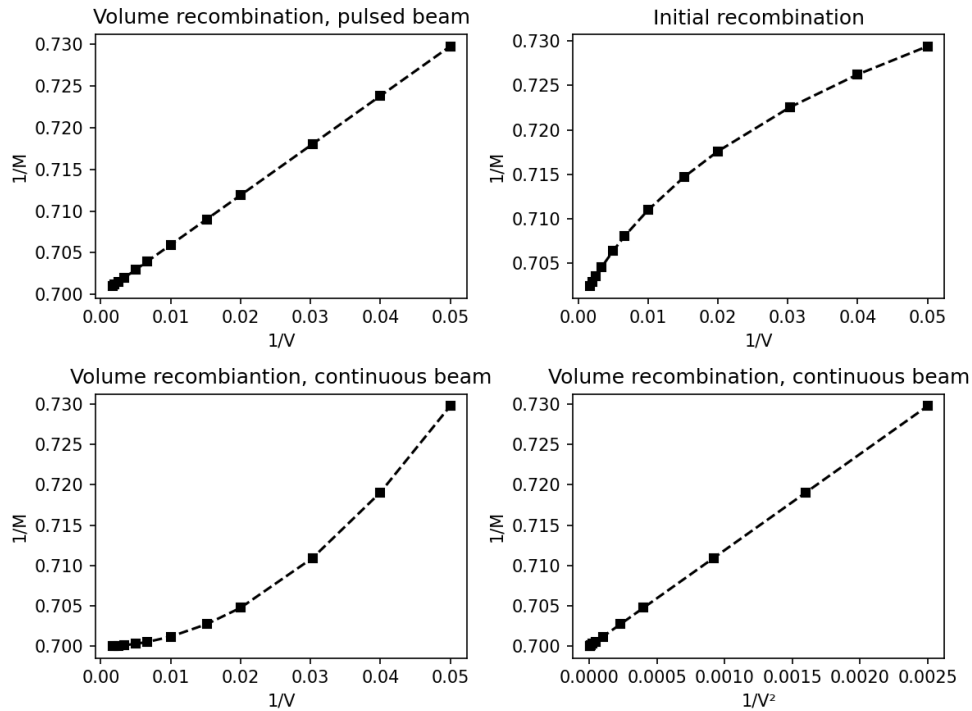


Figure 2.17: Examples of Jaffé plots ($1/M$ vs $1/V$ or $1/V^2$) corresponding to different recombination regimes.

As noted previously, modern PPCIs with reduced air gaps can exhibit charge multiplication effects. In such cases, Jaffé plots reveal two distinct regions corresponding to recombination and multiplication contributions (Figure 2.18). At low voltages (high $1/V$), the expected recombination trends dominate, while at high voltages (low $1/V$), the previous behavior is perturbed by the negative exponential behavior due to charge multiplication [68].

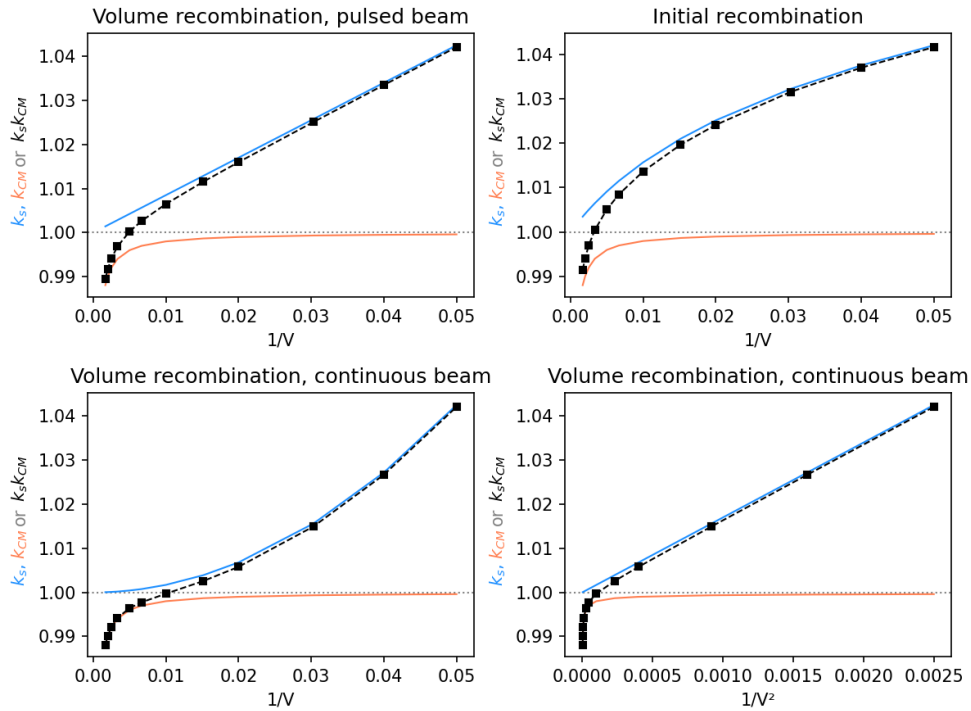


Figure 2.18: Illustration of the contributions of ion recombination (red) and charge multiplication (blue) to the overall response (black). The magnitude of charge multiplication corresponds to a typical PPIC of 1 mm gap thickness.

k_s can be determined by linear extrapolation or interpolation, based on a fit through multiple voltages without requiring the operating voltage to lie within the linear region:

$$k_s = \frac{M_{sat}}{M_N}, \quad (2.69)$$

where M_{sat} is the saturation charge and M_N the measured charge at the operating voltage. Figure 2.19 illustrates this method graphically.

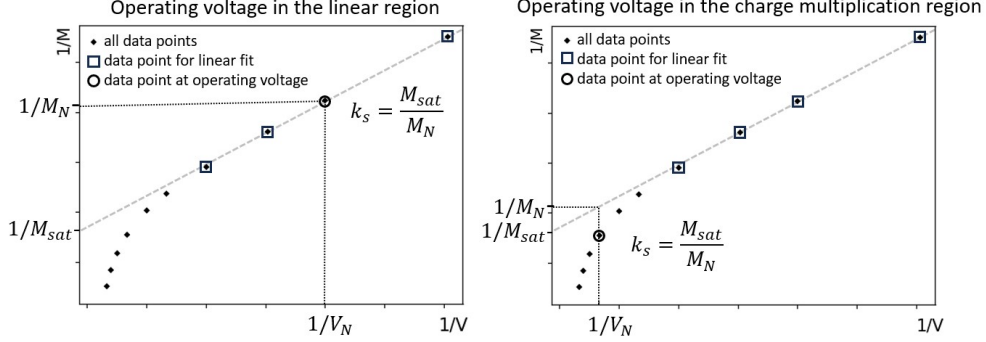


Figure 2.19: Representation of the Jaffé plot method. Interpolation or extrapolation is performed to estimate the collected charge at the operating voltage. Adapted from [68].

A drawback of the Jaffé plot method is its time-consuming nature: multiple measurements at multiple voltages must be measured under stable conditions. Each voltage change may disturb charge equilibrium in the chamber, requiring pre-irradiation with a dose of 2–10 Gy [151], which can take several minutes.

To reduce measurement effort, intermediate methods such as the three-voltage method (3VM) have been proposed [161]. This technique estimates M_{sat} by measuring $1/M$ at three voltages within a linear region. The recombination correction factor k_s is then obtained as the ratio between M_{sat} and the charge collected at the operating voltage, even if the latter is outside the linear region. The 3VM may be considered a good compromise between the two-voltage method and the Jaffé plot, as the additional measurement provides a check on linearity.

Currently, codes of practice provide no guidance for UHDR beams, which remain under investigation. The Jaffé plot method and the 3VM have both been demonstrated to be valid for UHDR proton beams delivered by isochronous cyclotrons. To date, there is a lack of experimental data characterizing UHDP proton beams. For UHDP conditions with electrons, the situation is more complex: extremely high instantaneous dose rates and space charge screening can distort the electric field and invalidate linear behaviors. Recently, a semi-empirical model based on a logistic function fit has been proposed, originally by Petterson [150] and later generalized [29] to arbitrary gap sizes:

$$k_s = \left(1 + \left(\frac{DPP}{V \cdot d^{-2}} \right)^\gamma \right)^\beta \quad (2.70)$$

where DPP is the dose per pulse (mGy), V the applied voltage (V), d the electrode spacing (mm), and γ and β fitting parameters. Although this model successfully describes charge collection losses, it still requires multiple measurements and careful fitting, making it relatively time-consuming. The associated uncertainty for this method is reported as 2.2% for an specific IC, and 3.7% for a general IC model.

Chapter 3

Simulation of ionization chamber efficiencies

This chapter describes the development of an in-house Monte Carlo simulation to model ion transport and recombination processes in ionization chambers. It presents the validation of the simulation tool against established theoretical models and experimental data. The content presented in this chapter corresponds to the published article: [Monte Carlo simulation of initial and volume ion recombination correction factor in plane parallel ionization chambers exposed to ion beams](#). Phys. Med. Biol. 69 165012, 2024.

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Summary

Objective: Accurate reference dosimetry with ionization chambers (ICs) relies on correcting for various influencing factors, including ion recombination. Theoretical frameworks, such as the Boag and Jaffé theories, are conventionally used to describe the ion recombination correction factors. Experimental methods are time consuming, the applicability may be limited and, in some cases, impractical to be used in clinical routine. The development of simulation tools becomes necessary to enhance the understanding of recombination under circumstances that may differ from conventional use. Before progressing, it is crucial to benchmark novel approaches to calculate ion recombination losses under known conditions. In this study, we introduce and validate a versatile simulation tool based on a Monte Carlo scheme for calculating initial and volume ion recombination correction factors in air-filled ICs exposed to ion beams with clinical dose rates.

Approach: The simulation includes gaussian distribution of ion positions to model the distribution of charge carriers along the chamber volume. It accounts for various physical transport effects, including drift, diffusion, space charge screening and free electron fraction. To compute ion recombination, a Monte Carlo scheme is used due to its versatility in multiple geometries, without exhibiting convergence problems associated with numerically solved procedures.

Main results: The code is validated in conventional dose rates against Jaffé's theory for initial recombination and Boag's theory for volume recombination based on parameters derived from experimental data including proton, helium and carbon ion beams measured with a plane parallel IC.

Significance: The simulation demonstrates excellent agreement, typically 0.05% or less relative difference with the theoretical and experimental data. The current code successfully predicts ion recombination correction factors, in a large variety of ion beams, including different temporal beam structures.

3.1 Introduction

Air filled ionization chambers (ICs) are one of the most accurate and reliable dosimeters to determine the absorbed dose in radiotherapy. They are extensively used in clinics and international dosimetry codes of practice such as IAEA TRS-398 [8] and AAPM TG-51 [10] endorse their use as the preferred detector for reference dosimetry and daily quality assurance in electron, photon, proton and heavier ion beams.

ICs measure the charged ion pairs created by the ionizing radiation inside the cavity of the detector. However, due to recombination, some of these ions do not reach the electrodes, leading to an underestimation of the collected charges. To compensate for this effect, an ion recombination correction factor (k_s) is applied to the response of the IC.

Ion recombination is a complex mechanism influenced by a variety of parameters, including particle type, beam quality, linear energy transfer (LET), depth, voltage, dose rate, beam delivery method and IC design. Generally, two types of recombination are recognized: initial and volume recombination. Initial recombination (intra-track recombination) occurs between ions within the same track or same trail of ionized species left behind the incident radiation particle, and it is theoretically addressed in the Jaffé model [88]. This type of recombination is heavily influenced by the LET of the particle.

In contrast, volume or general recombination is produced between ions of different tracks (inter-track recombination). It is described in the Boag models (for pulsed beams in [19], and in [23] for continuous beams) and is mainly dependent on the dose rate. In 1996, Boag extended his theory for pulsed beams to account for the fraction of electrons that do not attach to other molecules [22], known as the ‘free electron effect’. There are three updated models, each of them corresponding to different approximations of the distribution of electrons inside the IC. All three models estimate lower recombination compared to the original expression and depend on the free electron fraction, p :

$$p = \frac{1}{ad}(1 - e^{-ad}) \quad (3.1)$$

being d the distance between electrodes in plane-parallel geometry and a a coefficient that depends on the gas and the electric field strength. This coefficient a can be calculated as the inverse of the product of the mean time until attachment of the electron and the drift velocity of the free electron in the gas. These values depend on the electric field [106] and can be calculated from a fitting to the experimental data from [76].

Several methods have been developed to experimentally determine k_s , among them, the widely known two-voltage method (2VM), the recent three-voltage method by Rossomme et al. [161] or the approach developed by Boutillon et al. [31] based on De Almeida and Niatel method [130] and extended by Palmans et al. [142]. The 2VM is a reliable and accurate technique extensively tested and validated in electron and photon beams and is the standard method recommended by IAEA TRS-398 and AAPM TG-51. It is based on a first-order term of a series expansion around $1/V = 0$ of Boag's theory, in which the equation for k_s can be simplified as a linear relation between k_s and the inverse of the applied voltage ($1/V$) for pulsed beams or $1/V^2$ for continuous beams. Due to this approximation, the 2VM is only valid when the measured current is close to the saturation current.

For protons and ion beams, dense track cores result in variations in charge distributions, and the contribution of initial recombination can disturb this linearity [142]. In particle beams, the use of the 2VM is often limited [161] and alternative methods such as the Boutillon approach [31] are needed. That latter allows to determine experimentally the contribution of initial and volume recombination in a continuous beam by measuring the inverse of the charge collected by the IC versus the inverse of the voltage (these charts are frequently referred to as Jaffé plots) for three different dose rates. However, this method is time-consuming and hardly feasible in clinical routine, leaving linear methods as the only practical way to account for recombination.

Simulations are an accurate and time-efficient tool to comprehend recombination losses in cases that deviate from the conditions in which experimental methods or theories were intended and may not be valid. They can also help to find strategies to minimize recombination by making easy to explore different combinations of geometry and applied voltage.

In recent years, various simulations have emerged, primarily based on the resolution of partial differential equation systems (PDEs) that describe the temporal evolution of charge within the IC. [147] accurately predicts the complex chamber response for electron beams by assuming a homogeneous distribution of ions and solving the PDEs in one dimension. However, this approach is not suitable to model ion beams because the non-uniform gaussian distribution of the ion pairs generated in the IC does not allow the reduction of the dimensions of the problem. In [40] the PDEs resolution is extended to three dimensions, allowing to model initial and volume recombination in proton beams.

However, when dealing with complex geometries, the election of the mesh to solve the PDEs may be challenging and convergence issues with the resolution of

the PDEs may arise. To avoid these potential problems, [63] proposed a Monte Carlo simulation method that demonstrates its versatility across various geometries and any charge density distribution. However, their work focuses on calculating volume recombination in different geometries by assuming homogeneous ion distributions and exclusively models ion drift as the transport mechanism through the IC.

In this work, we present a Monte Carlo based simulation to model k_s for ion beams addressing both initial and volume recombination. The simulation includes Gaussian ion track structure and allows to generalize for any ion beam, energy spectrum and temporal structure of the beam. It includes transport mechanisms of charge carriers inside the IC like drift, diffusion, free electron fraction and space charge screening (SCS). These last two effects are believed to be crucial in the ultra-high dose rate (UHDR) regime. The inclusion of all these fundamental processes effectively models the behavior of ions inside IC. The simulation is tested for proton, helium and carbon beams and validated against Jaffé's theory for initial recombination and Boag's theory for volume recombination in pulsed and continuous beams in conventional dose rates. The parameters used in the calculations of both theories were obtained through fitting them to experimental data obtained from several experimental campaigns at different irradiation facilities measured with a plane parallel IC [163].

3.2 Materials and methods

The distribution of charge carriers created by an incident radiation particle is modeled using Jaffé's theory for initial recombination in combination with Boag model for volume recombination and the extended versions which account for the free electron fraction. The simulation methodology will follow the approach proposed by [63]: the algorithm starts by placing the charge carriers inside the active volume of the chamber. Every time step, the charges are shifted to account for the different transport processes, then the recombination algorithm takes place for every ion in the simulation. To simulate initial recombination only one track is computed and developed in the simulation, whereas for volume recombination various tracks are added in different time distributions, depending on the time structure of the beam. The previous steps are repeated until all charge carriers have been collected. At the end of the simulation, the number of ions reaching the electrodes are counted, and k_s is computed as the number of ions initially created divided by the number of ions collected by the electrodes.

The non-homogeneous distribution of charge carriers created by ion beams does not allow the reduction of the dimensions of the problem. Therefore, the simu-

lation is carried out in 3D. For modeling k_s of a specific beam, it is necessary to provide the beam's LET, dose rate, chamber geometry and voltage applied. Further details about the distribution of charge carriers, the transport process, the recombination scheme, dose rate implementation and uncertainties are given in the following sections (3.2.1 - 3.2.5).

3.2.1 Implementation of the charge carrier distribution on a single track

When the incident particle passes through the detector and ionizes the sensitive material in its track, it creates a non-homogeneous distribution of positive and negative charge carriers. Based on Jaffé's theory for column recombination [88], the charge carriers in the simulation follow a cylindrical distribution with a radial gaussian profile (see Figure 3.1) with the width of $b^2 = 2\sigma^2$ (σ is the standard deviation of the Gaussian distribution) centered at the trajectory of the incoming particle. This gaussian charge carrier density $n_0(R)$ inside the cavity ($0 < z < d$) is proved to be the best correlation with experimental data [92] and is modeled as:

$$n_0(R) = \frac{N_0}{\pi b^2} e^{-\frac{R^2}{b^2}} \quad (3.2)$$

where N_0 is the linear charge carrier density that can be obtained as the ratio between the LET of the particle beam and the mean energy expended to form an ion pair in air by the incident radiation particle ($\bar{w}_{air}$). The parameter b is the initial mean square radius, which can be provided by the user, or if it is unknown, it can be calculated with the LET of the particle with the following experimental relation [163]:

$$b(\cdot 10^{-3}) = -0.393 \cdot \log[10^{-3} \cdot LET]^2 + 3.094 \cdot \log[10^{-3} \cdot LET] - 0.584 \quad (3.3)$$

Where LET is in $\text{KeV } \mu\text{m}^{-1}$ and b in cm. For low LET values, b is considered as a constant value of $10 \mu\text{m}$ [93]. For high LET values b reaches a saturation value of $50 \mu\text{m}$ [163].

The number of ions placed in each ion track is calculated as the product of N_0 and the length of the particle path inside the IC. Assuming that the ionizing particle enters perpendicular to the IC, the length of the particle path is equal to the air gap thickness of the plane parallel chamber.

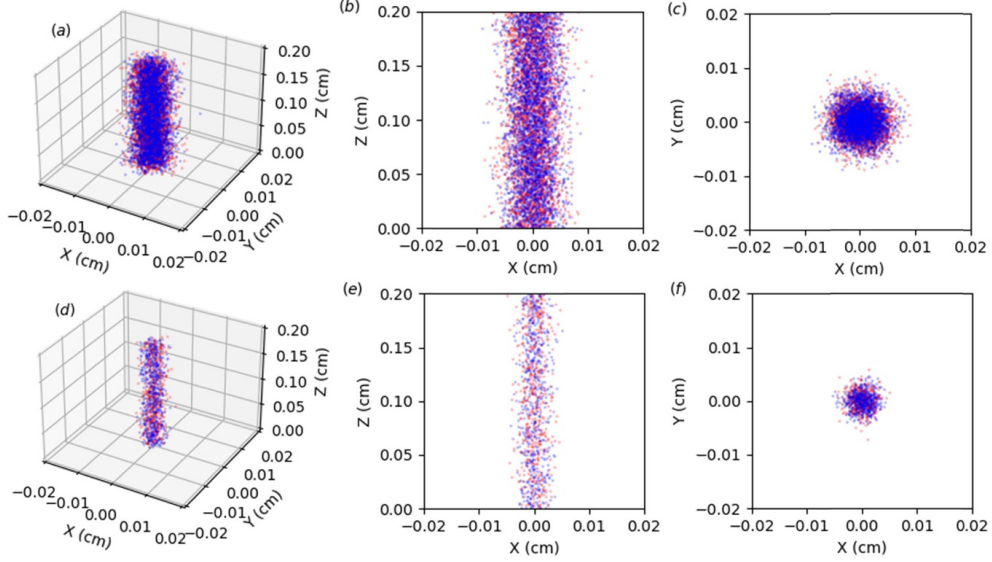


Figure 3.1: (a) 3D, (b) axial and (c) transversal view of the gaussian structure of a 115 MeV/u Carbon ion track. (d) 3D, (e) axial and (f) transversal view of the gaussian structure of a 96 MeV/u proton track. The blue points represent the negative charge carriers and the red points represent the positive charge carriers.

The negative charge carriers initially created by an incident particle consist of electrons. The negative ions will be formed when the electrons diffuse and attach to other molecules. Previous studies [25, 40, 147] have shown that recombination between electron and positive ions is negligible for ion beams as electrons are dragged out to the collecting electrodes orders of magnitude faster than the ions. Based on this, the electrons are assumed to be instantaneously collected, and the free electron fraction is considered as a lack of negative ions. Taken this into consideration, p is calculated from the parametrization in [106], and the three different models described by Boag [22] are implemented in the simulation as:

- *Model I*: The fraction of negative ions is reduced by a factor $1 - p$.
- *Model II*: Negative ions reduced by a factor $1 - p$ are distributed in the volume of the chamber between $z = pd$ and $z = d$.
- *Model III*: A fraction of negative ions $\sqrt{1 - p}$ is distributed between $z = (1 - \sqrt{1 - p})$ and $z = d$.

An illustrative example of the implementation is provided in Figure 3.2.

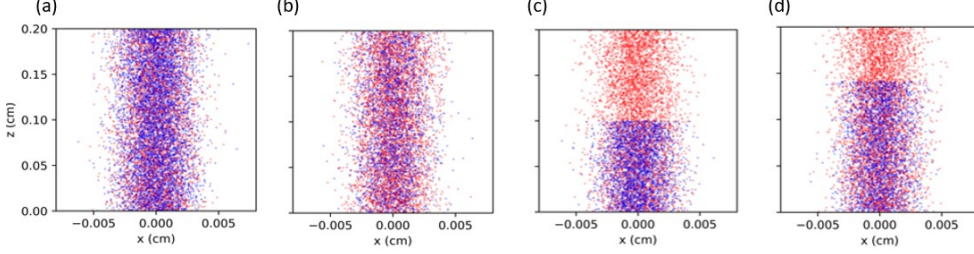


Figure 3.2: (a)–(d): Implementation of distribution of positive (red points) and negative ions (blue points) at $t = 0$ according to the different Boag models (0, I, II and III, respectively) in the simulation. All representations correspond to a 50% free electron fraction, $p = 0.5$.

3.2.2 Implementation of the transport algorithm

After the ions are placed in the simulation, each one is shifted in a straight line of distance $\Delta r_{\pm}$ each time step. The direction of this shift is determined by the vectorial sum of the three components $\Delta \vec{r}_{\pm} = (\Delta \vec{r}_{x,\pm}, \Delta \vec{r}_{y,\pm}, \Delta \vec{r}_{z,\pm})$. The modulus of the displacement of ions of z -component ($\Delta r_{z,\pm}$) is given by the following expression:

$$\Delta r_{z,\pm}(\Delta t) = \pm \mu_{\pm} E_z \Delta t \pm^* \sqrt{2D_{\pm} \Delta t} \mp \mu_{\pm} E_{SCS,z} \Delta t \quad (3.4)$$

The displacement in x and y axis is analogous. The first term from Equation 3.4 models the drift of ions, which depends on the mobility of positive and negative ions ($\mu_{\pm}$) and the electric field E_z . In plane parallel geometry, the electric field it is assumed to be constant and only has z -component: $\vec{E}(r) = \vec{E}_z = \frac{V}{d} \hat{z}$, where V is the bias applied voltage, d is the separation between plates and $\hat{z}$ the unit vector, perpendicular to the electrodes. The time step Δt is calculated as:

$$\Delta t = \frac{b}{\delta \cdot E \mu_{\pm}}$$

where δ is the number of discretizations in the time step, which may be adjusted by choosing a value > 1 to increase the time step resolution. The second term in Equation 3.4 represents the diffusion motion. To calculate how far the ion moved after a time Δt has elapsed, the square root of the mean squared displacement of the Brownian motion was used, $MSD = 2D_{\pm} \Delta t$. $D_{\pm}$ represents the ion diffusion constant of negative or positive ions. Note that the sign $\pm^*$ in Equation 3.4 implies that the diffusion is not always towards the same direction. After $|\sqrt{2D_{\pm} \Delta t}|$ is calculated, it is multiplied by randomly sampled -1 or 1. By doing this, the ions to move in random directions and eventually that leads to a naturally diffusion

towards lower concentration of ions. This term may produce that some charge carriers may go out of the lateral limits of the detector. In this case, they are equally collected and counted, with this we ensure that all the ions missing are due to recombination losses.

The third term corresponds to the SCS. It can be understood as a distortion of the electric field experienced by ions due to the presence of other charged species that screen the electric field caused by the potential difference between electrodes. This term can increase recombination as the charge carriers of opposite sign overlap longer. This effect is implemented with a term similar to the drift but with a perturbed 'screened' electric field $\vec{E}_{SCS,z}$ for every positive and negative ion located at z .

In this work, we exclusively consider the component of the screened electric field along the z -axis, as it is the vectorial component that perturbs the electric field in the direction of the collection motion. This simplification is made under the assumption that contributions from the x and y axis are negligible, primarily due to vectorial compensation near the central axis of the IC, caused by the circular geometry in the $x - y$ plane.

SCS may also alter the velocity of ions, given by $\vec{v} = -\mu_{\pm}\vec{E}^{eff}$, where $\vec{E}^{eff} = \vec{E} + \vec{E}_{SCS}$. This change in velocity could potentially affect the recombination probability, as the recombination constant arises from the product of the cross section (σ) and the relative speed between two ions i and j (v_{ij}): $\alpha \equiv \sigma \cdot v_{ij}$ [7]. However, due to the approximation of α being constant, this effect is not taken into consideration.

To calculate $E_{SCS,z}$, each track of ions is considered a cylinder of uniform charge density, the electric field is computed by integrating the contribution of each disc of the cylinder to the coordinates of the ion. To calculate the charge density in the integral, the number of ions contained on each disc is counted and multiplied by the elemental charge.

The values of the different constants used in the simulation can be found in Table 3.1.

Constant	Symbol	Value	Units	References
Average ion diffusion	$D_{\pm}$	0.037	$\text{cm}^2 \text{ s}^{-1}$	[93]
Average ion mobility	$\mu_{\pm}$	1.65	$\text{cm}^2 \text{ V}^{-1} \text{ s}^{-1}$	[22]
Ion recombination constant	α	$1.6 \cdot 10^{-6}$	$\text{cm}^3 \text{ s}^{-1}$	[19]
Mean energy to form an ion pair	$\bar{w}_{air}/e$	34.23 (protons) 35.72 (heavy ions)	J C^{-1}	[8]
Air density	ρ	0.001225	g cm^{-3}	[90]

Table 3.1: Parameters of the different constants used in the simulation. The use of the same diffusion and mobility parameters for positive and negative ions instead of more recent and accurate values such as [25] is justified as in this work the simulation is compared with fixed values in Jaff  and Boag theories which do not account for this distinction.

3.2.3 Implementation of the recombination scheme

The recombination is considered as a random process computed with a Monte Carlo scheme similar to [63] with some modifications which allow to reduce the computation time. The scheme consists on calculating the probability of recombination for each i th negative ion, then sampling a random number between 0 and 1. If the random number is smaller than the recombination probability and the distance between the i th negative ion and closest positive ions is less than the recombination radius, a recombination event occurs. As a consequence, the pair of positive and negative ions are annihilated.

The probability of recombination for the i th negative ion belonging to track k , on time step t , is calculated as:

$$P_{-}^i(t) = 1 - e^{-\alpha \cdot \rho_{+,k}(t) \cdot \Delta t} \quad (3.5)$$

where $\rho_{+,k}(t)$ is the local density of positive ions in the core of track k . $\rho_{+,k}(t)$ is calculated every time step as the number of positive ions inside a sphere of radius r_f , centered in the middle of track k divided by the volume of the sphere. The value of r_f is left as a free parameter, that is found to be optimal if it is set to $1.6 \frac{b}{\sqrt{2}}$ according to the best fit to the Jaff  theory for a 62 MeV/u carbon ion beam [162]. To avoid recombination between ions that are far apart the following constrain is added: if the distance between ions is bigger than r_f , the ions do not recombine.

Note that the data points marked with yellow triangles in Figure 3.3 correspond to the simplified Monte Carlo algorithm introduced in [63], where no r_f is considered and $\rho_{+,k}(0)$ is the same quantity as $n_0(R)$. In contrast, our approach accurately computes the probability of recombination without the need to con-

sider the local density of each ion, as required in the full Monte Carlo in [63], which demands higher computation time.

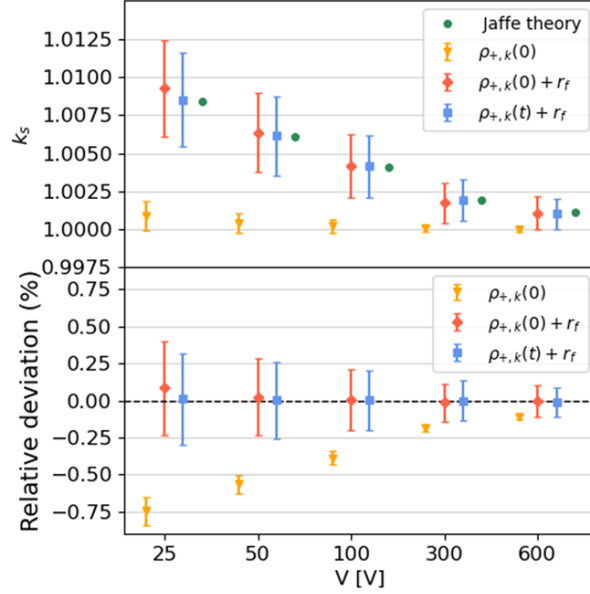


Figure 3.3: Relative deviation of the k_s values with Jaffé theory for different voltages when different approaches to calculate $P_-^i(t)$ are taken to calculate initial recombination. In yellow triangles no radius of action r_f is considered and $\rho_{+,k}$ is calculated for each track only at the beginning of the simulation. This is equivalent to the simplified Monte Carlo algorithm in [63]. In red diamonds the radius of action is included and $\rho_{+,k}$ is calculated only at the beginning of the simulation. In blue squares the radius of action is included and the probability is calculated on each time step for each track. This last approach satisfactorily predicts the theoretical values with minimal relative difference, less than 0.01% for initial recombination in a proton beam.

The distinction between the red diamonds and blue squares in Figure 3.3 is attributed to the inclusion of the diffusion in the transport algorithm. Particularly at low voltages, ions exhibit greater diffusion, which leads to a reduction in the local density of ions. This shows the importance of including diffusion and the necessity of a 3D simulation for accurately simulating charge losses due to initial recombination.

3.2.4 Implementation of dose rate for volume recombination

To model initial recombination, one track is added and evolved in the simulation. For volume recombination the same scheme is followed but various tracks are placed randomly over time (TR , *Track Rate*) in the area of the simulation (πR_{sim}^2) according to the fluence rate ($\dot{\phi}$) that depends on the dose rate ($\dot{D}$) as proposed by [40]:

$$TR = \pi R_{sim}^2 \dot{\phi}, \quad \dot{D} = \dot{\phi} \left(\frac{\bar{S}_{en}}{\rho_{air}} \right) \quad (3.6)$$

The number of tracks needed to add to the simulation and their distribution over time depends on the dose rate and if the beam is considered pulsed or continuous. A beam is considered pulsed if the pulse duration is much shorter than the collection time of the IC and the latter is much shorter than the pulse repetition period. Considering this definition, the pulsed beam is simulated by inserting all tracks in the simulation homogeneously along the pulse duration and considering the instant dose rate of the pulse. A continuous beam is considered when the beam does not fulfill the previous definition. In this case, the average dose rate is considered and the tracks are inserted following a homogeneous distribution over the simulation time. Due to computation limitations, only a fraction of the IC volume is simulated ($R_{sim} \sim R_{IC}/10 \sim 0.8$ mm). Figure 3.4 shows how the ion tracks are sampled all over the area of the simulation according to the different dose rates.

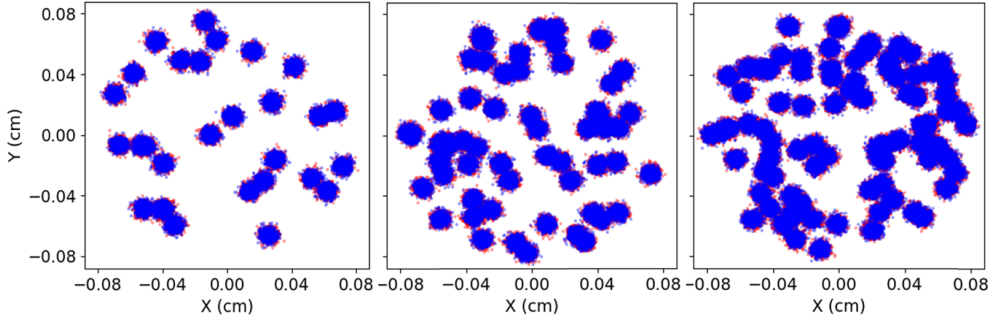


Figure 3.4: Distribution of Carbon Ion tracks over the transversal section of the IC for 3 dose rates (DR): 0.3·DR, 0.6·DR and DR (corresponding to ~ 16 Gy/min) of a continuous Carbon Ion Beam (from left to right). Each cluster of points represents a column of ions as shown in Figure 3.1.

3.2.5 Uncertainties

Monte Carlo methods are used in almost every phase in the simulation, from randomly sampling the initial distribution of ion pairs, to modeling recombination and calculating the shift on the position of ions due to stochastic effects like diffusion. Due to the inherent randomness of the processes being modeled and to reduce the noise typically associated with this method, the k_s value is obtained by repeating the simulation several times and averaging the results over the multiple batches.

The type-A uncertainty of the Monte Carlo simulation is calculated as the standard deviation of all k_s divided by the square root of the number of batches. Type-B uncertainties emerge as the most significant source of uncertainty. The contribution of various sources to the overall uncertainty, which is found to be 0.9%, is explicitly addressed in Table 3.2. To estimate the relative standard uncertainty, the impact of the maximum and minimum values found on literature of the different sources of uncertainty to a general case was calculated: a 96.17 MeV proton beam with a 2 mm air gap chamber with a voltage of 300 V at a dose rate of 20 Gy/min. It is anticipated that for UHDR or higher k_s values, the uncertainty will be larger.

Sources of uncertainty	Range of values / variability	U (%)
$\mu_{\pm}$, Average ion drift coefficient ($\text{cm}^2 \text{V}^{-1} \text{s}^{-1}$)	1.98 - 1.6	0.1
$D_{\pm}$, Diffusion coefficient ($\cdot 10^{-2} \text{cm}^2 \text{V}^{-1} \text{s}^{-1}$)	3.7 - 3.59	0.1
α , Ion recombination constant ($\cdot 10^{-6} \text{cm}^3 \text{s}^{-1}$)	0.9 - 1.6	0.3
N_0 , Linear charge carrier density (ions/cm)		
LET ($\text{KeV } \mu\text{m}^{-1}$)	$\pm 10\%$	0.6
$\bar{w}_{air}/e$ (J C^{-1})	$\pm 1.5\%$	0.1
b , gaussian radius (mm)	± 0.001	0.3
p , Free Electron fraction		
a (cm^{-1}) ¹	$\pm 1.5\%$	0.1
Boag model	Model 0 / Model II	0.1
Dose Rate (Gy/min)	± 10	0.4
Voltage		
300 V	± 1	0.1
30 V	± 1	0.3
d , Air gap thickness (mm)	± 0.1	0.1
Combined	-	0.9

Table 3.2: Sources of type-B uncertainty, range of values found on literature or typical variability and the relative standard uncertainty (U) associated in conventional dose rates.

¹To quantify the variability of a , the parametrizations from [25] and [106] were used.

To calculate k_s for initial recombination, a minimum of 1000 batches were conducted to achieve accurate results (see Figure 3.5), resulting in type-A uncertainties lower than 0.2% in all cases. For volume recombination and high LET beams, where a large number of ions are simultaneously present in the simulation, a dramatically reduced number of iterations is needed.

The present algorithm is implemented in python. The simulation of a single track with 512 ions pairs of a 96 MeV proton beam in a space gap of 2 mm at 300 V, iterated 1000 times takes 117 s with a single threaded laptop with Intel i7 processor, 2.5 GHz and 32 GB RAM. Simulation time of volume recombination depends on the dose rate. One single iteration of the previous pulsed beam at the same voltage, with a reduced radius of $R_{IC}/10$ (more information on section 3.2.4), and a beam intensity of $2.9 \cdot 10^9$ particles/s which corresponds to 24,576 ion pairs initially created in the simulation takes 205 s.

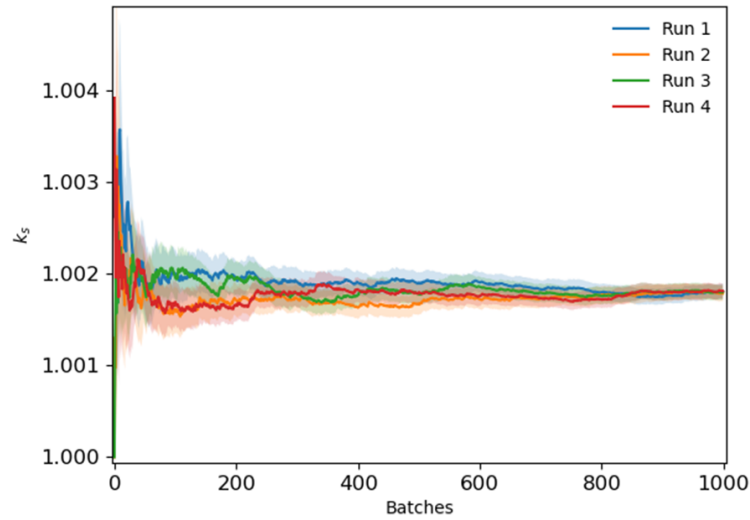


Figure 3.5: Evolution of various collecting histories of the k_s averaged and standard deviation bands of the mean over the number of batches for a proton beam with 512 ions/track at 300 V. The number of batches needed to achieve a stable result is inversely proportional to the number of ions present in the simulation. The different runs converge to the same value.

3.2.6 Experimental setup for code validation

To validate the numerical code, k_s values for different beams and voltages were computed based on parameters from published experimental data for proton, helium and carbon beams [163]. All measurements were performed with an IBA PPC40, with an air gap size of 2 mm, addressing the widest range of voltages

used in literature for both clinical and research purposes: 20 – 600 V. Through the Jaffé plots experimentally obtained and fittings to Boag and Jaffé models, specific values of b , N_0 , $\bar{q}$ and q (see Equations 2.21, 2.27 and 2.51) were found for each ion beam. With these parameters, theoretical k_s values for each ion beam were determined and compared with our numerical results.

For the experimental results used to validate the simulation a 96.17 MeV non-modulated pulsed pencil beam scanning (PBS) proton beam produced by a synchro-cyclotron was used. The pulsed repetition frequency was 1 kHz and the pulse length varied between 4 – 6 μ s. Heavier ion beams in continuous mode were also investigated. A 50.57 MeV/u PBS helium beam produced by a synchrotron. The spill duration was in the range of 5 s and the pause between spills was 4.5 s. A 115 MeV/u PBS carbon ion beam measured at the plateau and spread out Bragg peak (SOBP) produced by synchrotron, with spill duration between 1–3 s and pause between spills 4–5 s. More details can be found in [163].

3.3 Results and validation

3.3.1 Proton beam

For the 96.17 MeV pulsed PBS proton beam, the parameters used to model the track structure were: $N_0 = 2559$ ions/cm and $b = 0.00225$ cm according to the values that can be found in [163]. In Figure 3.6 (a) it can be seen that the results for initial recombination are in good agreement with Jaffé theory, the relative differences between theoretical values and the Monte Carlo simulation for the different voltages were below 0.05%.

In Figure 3.6 (b), results for six doses per pulse were compared to verify that the simulation can satisfactorily compute volume recombination for the following dose rates: $0.5 \cdot \dot{D}_{inst}$, $1.7 \cdot \dot{D}_{inst}$, $1.92 \cdot \dot{D}_{inst}$, $3.33 \cdot \dot{D}_{inst}$ and $6.21 \cdot \dot{D}_{inst}$, with $\dot{D}_{inst}$ the dose rate per pulse corresponding to $2.9 \cdot 10^9$ particles/s as defined in [163]. According to Equation 3.6, $\dot{D}_{inst}$ is found to be on the order of 20 Gy/min. Volume recombination can be calculated independently if the condition of only allowing recombination between ions from different tracks is added. To calculate both volume and initial recombination at the same time in the simulation, no constraint is added. All the computed k_s values are in accordance with Boag theory. If the free electron fraction (e.g. $p = 0.24$ at 300 V) is considered, small relative differences were found only at high voltages: at 500 V, 0.05% with Boag model I, 0.08% with Boag model II and 0.07% with Boag model III. As there is no consensus on which model is the most accurate and the relative difference were very small, no free electron fraction was considered. Similar differences were found

for all the other cases shown in this work. Values of the uncertainty (type-A) were found to be 0.02% or smaller.

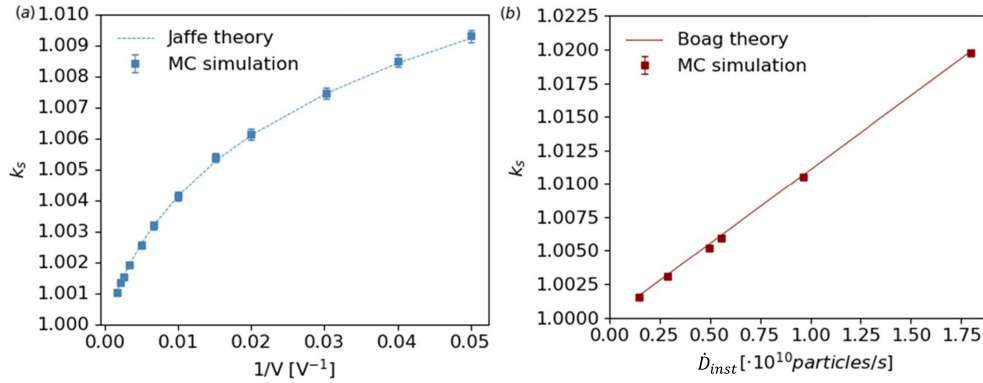


Figure 3.6: (a) k_s versus inverse of the voltage for a 96.17 MeV proton beam. Comparison between Jaffé theory (blue dashed line) and Monte Carlo simulation (blue solid squares) for initial recombination. (b) k_s versus the dose rate per pulse ($\dot{D}_{inst}$) at 300 V. Comparison between Boag (red solid line), neglecting the free electron fraction, and Monte Carlo simulation (red solid squares) for volume recombination in a pulsed proton beam.

3.3.2 Helium beam

For the 50.57 MeV/u quasi-continuous PBS Helium beam, the parameters used for the track in the simulation were: $N_0 = 1739$ ions/cm and $b = 0.00137$ cm according to the calculations that can be found in [163]. At 0.67 cm water equivalence depth (in the plateau) three dose rates were used: DR, $0.66 \cdot DR$ and $0.5 \cdot DR$. For this beam, the absolute dose rate values within the phantom were not available due to the complexity of the definition of the dose rate in PBS modalities. [163] primarily relied on the relative values, which is similarly done in this work by scaling the dose rate values. In the pulsed proton beam from previous section, it was possible to validate the k_s values related to certain levels of dose rate. These values served to obtain a rough estimation of the dose rate levels of the other beams according to Equation 3.6. In this case, the average dose rate (DR) was found to be of order of 3 Gy/min.

Figure 3.7 (a) shows a comparison between numerical and theoretical k_s -values for the three dose rates. The uncertainty values (type-A) ranged from 0.05% to 0.01%, the highest values were found for the initial recombination or low dose rates where less ions are involved.

In Figure 3.7 (b), numerical values are compared to theoretical values for the dose rate DR, when initial and volume recombination are both present and their contribution. The total theoretical k_s is calculated as the product of Jaffé theoretical value and Boag theoretical value: $k_{s,theo}^{total} = k_{s,Jaffe}^{ini} \cdot k_{s,Boag}^{vol}$.

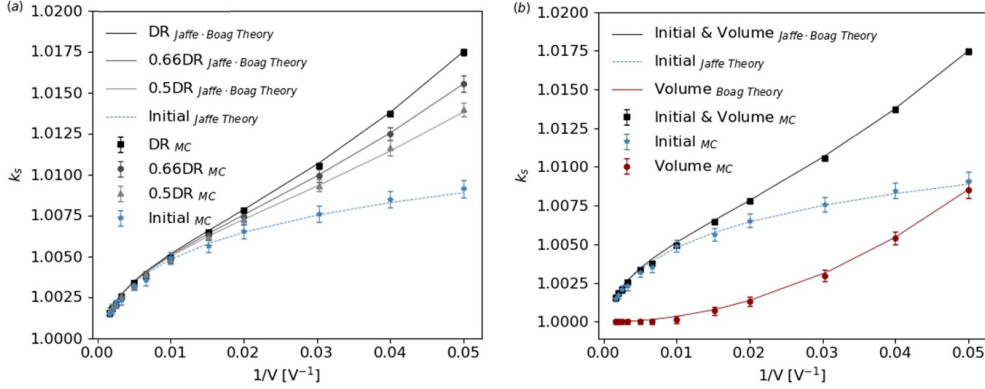


Figure 3.7: (a) Comparison between theoretical values on solid curves and MC simulation on solid symbols for three different dose rates: DR, 0.66·DR and 0.5·DR with the contribution from initial recombination (blue). (b) Contribution of initial and volume recombination (for the dose rate DR) to the total k_s versus inverse of the voltage for a 50.57 MeV/u Helium beam. The solid red circles show the MC calculation of the volume recombination contribution and on solid red curve the theoretical values from Boag theory. The solid blue stars show the MC calculation of initial recombination and on the dashed blue curve the theoretical values from Jaffé theory. The solid black squares show the MC calculation of the total recombination and on the solid black curve the theoretical values that can be obtained from multiplying Jaffé and Boag theories.

3.3.3 Carbon beam

To model a 115 MeV/u quasi-continuous PBS Carbon Ion beam in the plateau, the parameters used in the simulation were: $N_0 = 9565$ ions/cm and $b = 0.00345$ cm. Figure 3.8 (a) shows k_s values for the three dose rates tested: DR, 0.6·DR and 0.3·DR. As done for the helium beam (see section 3.3.2), the average dose rate (DR) was estimated to be 16 Gy/min.

To model the same beam in the middle of the SOBP the parameters used in the simulation were: $N_0 = 15478$ ions/cm and $b = 0.0037$ cm. Figure 3.8 (b) shows the tested dose rates: DR and 0.6·DR, where DR $\approx$ 26 Gy/min. All the results are in accordance with theoretical values. Values of the uncertainty (type-A) were found to be 0.1% or smaller.

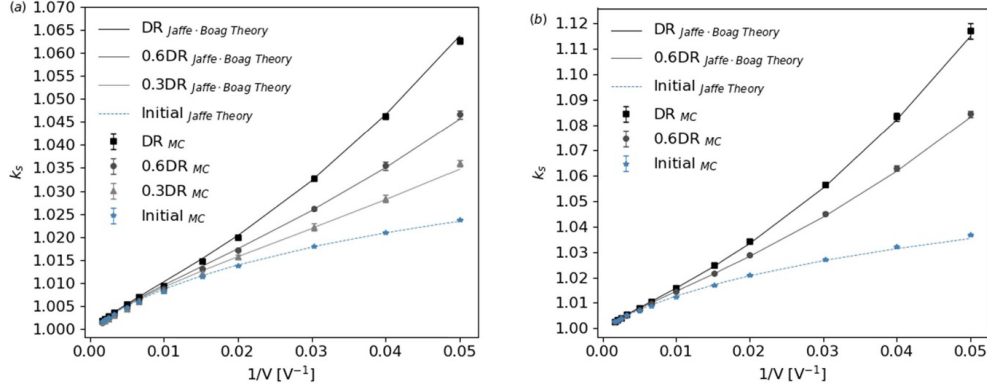


Figure 3.8: k_s versus inverse of the voltage of a 115 MeV/u Carbon ion beam. (a): Comparison between Jaffé, Boag theoretical values (solid lines) and numerical values (symbols) for different dose rates at the plateau. (b): Analogous graph for the SOBP beam.

3.3.4 Space charge effect

With the emergence of a new treatment modality known as FLASH therapy, that requires UHDR conditions, there is a growing interest in investigating the response of ICs in this regime. When the dose rate is significantly increased, it has been observed that the Boag theory is not in accordance with the simulated [147] and experimental values [150]. This trend suggests that the Boag theory is not suitable for UHDR conditions due to the non-inclusion of the SCS.

Figure 3.9 (a) illustrates the difference in k_s values with and without the inclusion of space charge. It is predicted that for PPC40, Boag theory will start to fail if the dose per pulse is increased by approximately one order of magnitude compared to the dose rates in the pulsed proton beam used in this work. Figure 3.9 (b) shows the distortion of the electric field along the IC air gap according to the distribution of ions proposed in Boag model III. At low dose rates, as used in this work, the screened electric field is negligible (purple line). As the dose per pulse increases, the electric field becomes more and more screened. A 10% relative difference in k_s value was found at $4.25 \cdot 10^{11}$ particles/s (Figure 3.9 (a)), where the maximum distorted electric field reaches a 40% difference from the bias electric field (Figure 3.9 (b)). Figure 3.9 (c) shows that the choice of Boag model significantly affects the distribution of the distorted electric field due to SCS, however the impact on k_s of each model was found to be similar as in conventional dose rates. This should be thorough studied for other beams and other conditions.

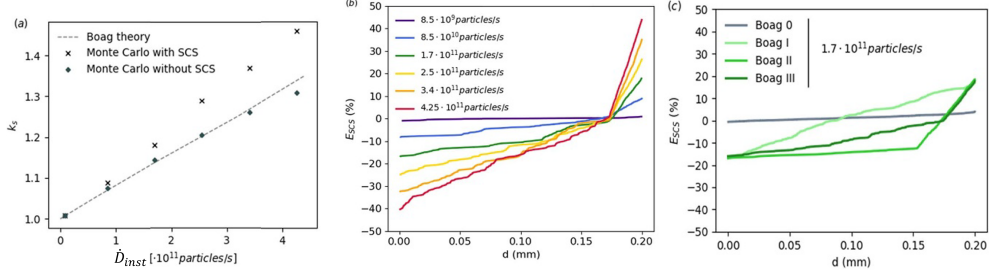


Figure 3.9: (a) k_s values for a PPC40 versus $\dot{D}_{inst}$ at 300 V for a pulsed proton beam. Comparison between Boag theory (dashed gray line) and Monte Carlo simulation if the SCS is included in the simulation (black crosses) and if the SCS effect is not included (dark grey solid diamonds). (b) Distortion of the electric field relative to the bias electric field (1500 V/cm) along the air gap for different dose rates according to Boag distribution of free electrons III. (c) Impact on the SCS distribution of the different Boag models at $t = 0$ for $1.7 \cdot 10^{11}$ particles/s.

3.4 Discussion and conclusion

In this study, we have presented a new Monte Carlo simulation code that effectively models the ion recombination factor for plane parallel IC exposed to clinical ion beams (quasi-continuous helium and carbon ion beams and pulsed proton beams). Our simulation demonstrated excellent agreement (typically 0.05% or less relative difference) with established theories, such as Jaffé theory for initial recombination and Boag theory for volume recombination regardless of the temporal beam structure.

We have also introduced a novel approach to compute recombination, significantly reducing simulation time compared to previous works. This enables three-dimensional calculations necessary to model initial recombination and its interplay with volume recombination in a reasonable time. While our implementation considered effects like diffusion, free electron fraction and SCS, validation with experimental data showed that the free electron fraction and the SCS term are negligible due to the air gap thickness, the low dose rates and dose per pulse conditions addressed in this work.

Further investigations with experimental values are needed to benchmark the simulation in the UHDR rate regime where Boag theory fails. This simulation tool holds the potential to extend k_s calculations beyond these limits. Other effects, such as the charge multiplication, should be further investigated as it could potentially interplay with the free electron fraction and SCS.

Chapter 4

Study of materials for UHDR

This chapter presents an experimental study of materials exposed to prolonged UHDR conditions, describing the irradiation protocols, characterization methods, and performance assessment, concluding with recommendations for dosimetric device construction. The content presented in this chapter corresponds to the published article: [Radiation damage evaluation of materials for radiotherapy quality assurance devices under high dose and ultra-high dose rate electron and proton beams](#). Phys. Med. Biol. 70 165018, 2025.

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Summary

Objective: FLASH radiotherapy is a promising technique based on the delivery of ultra-high dose rates (UHDR) to spare healthy tissue. Robust quality assurance (QA) is required to ensure a safe delivery of the treatment. QA devices such as phantoms and ionization chambers are typically made out of polymeric materials to ensure water equivalence. However, radiation exposure, particularly at UHDR where achieving high doses is easier, may cause irreversible changes to the structure of these materials. Such extreme conditions can, for example, induce microstructural defects that may lead to mechanical failure or alter electrical properties such as the dielectric permittivity or conductivity, potentially compromising the calibration and reliability of critical QA devices, such as ionization chambers. This study aims to characterize radiation damage in common materials used for QA devices and identify which of them can withstand these challenging conditions.

Approach: A variety of materials commonly used in phantoms and ionization chambers, with diverse characteristics (transparent, opaque, conductive and non-conductive) were irradiated using 68 MeV proton and 20 MeV electron beams, reaching doses up to 1 MGy under UHDR conditions (average dose rates of 100 – 500 Gy/s). Material damage was evaluated through optical, chemical, mechanical and electrical tests to quantify change in different properties.

Main Results: External appearance of some materials significantly changed after irradiation. All transparent materials exhibited change in color post-irradiation. Chemical analyses conducted after irradiation and repeated two years later indicated partial recovery in some materials. No significant difference in damage was observed between proton and electron irradiation, suggesting comparable radiation damage mechanisms. Dose rate alone did not exacerbate damage beyond total dose effects; however, extended irradiation at high dose rates resulted in thermal damage under some conditions. Mechanical testing revealed increased fragility, changes in hardness and dimensions, while some materials experienced significant changes in dielectric constant and conductivity.

Significance: Materials such as *Polymethyl Methacrylate* (PMMA), *Polycarbonate* (PC), *Polyoxymethylene* (POM), and its electrically conductive variant POM ELS, are unsuitable for prolonged irradiations at UHDR due to significant structural degradation observed. For see-through phantom construction, *Clear Polystyrene* (CPS) offers a more durable alternative to PMMA. For detector construction, *Polyether ether ketone* (PEEK, endorsed for non-conductive parts) and graphite (for conductive parts) demonstrated promising durability, making them preferable choices under high dose and UHDR conditions.

4.1 Introduction

Polymeric materials are widely employed in the field of radiation therapy, particularly in the construction of quality assurance (QA) devices such as ionization chambers (ICs), water tanks, and phantoms. These materials are preferred due to their unique properties, including mechanical strength, radiation resistance, and water equivalence, a key property for accurate dose measurements, as emphasized by the International Atomic Energy Agency (IAEA) protocol TRS-398 [8].

FLASH radiotherapy, an emerging cancer treatment modality, delivers therapeutic doses at ultra-high dose rates (UHDR), several orders of magnitude higher than those used in conventional radiotherapy ($\gtrsim 40$ Gy/s [194]). This promising technique has demonstrated to spare healthy tissues while effectively controlling tumors and has been observed with different particles [52, 125]. UHDR conditions poses several challenges, [50, 176], including material selection for QA devices, as high doses are easily achieved in a short time, accelerating the material degradation. When polymeric materials are irradiated, they undergo complex chemical and physical processes, including macromolecular chain scission, cross-linking, and free-radical formation [60]. Over time, these processes result in cumulative defects that may degrade the material's properties. This degradation may be particularly pronounced under UHDR conditions, as illustrated in Figure 4.1, where significant degradation of commercially available ICs and water phantoms exposed to UHDR is shown.

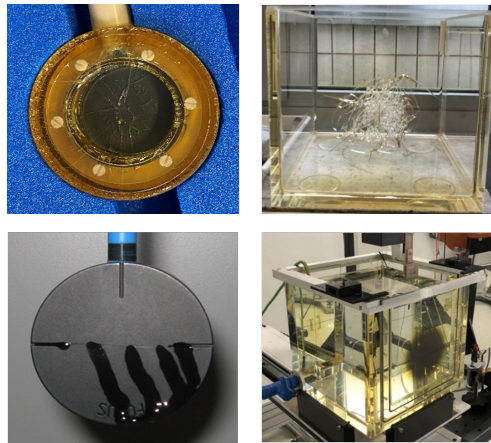


Figure 4.1: Commercial ICs (Top: IBA PPC40, Bottom: PTW ROOS Chamber) and in-house built water phantoms (Top: built out of PMMA, Bottom: built out of Polycarbonate) after exposure to very high dose and ultra-high dose rates with an electron beam observed at Physikalisch-Technische Bundesanstalt (PTB).

The functional requirements of QA materials vary depending on their application. Transparency is essential for devices such as water tanks and phantoms, where precise alignment with positioning laser systems is critical. In contrast, materials used in ICs do not require optical clarity. But they require durability and a combination of conductive and non-conductive components. These differing characteristics require the selection of polymers tailored to their specific applications. Given the importance of QA devices in ensuring the safe delivery of radiotherapy, it is vital to understand the limits of radiation-induced degradation of materials used in their construction.

Assessing changes in optical, mechanical, chemical, and electrical properties is crucial, as irradiation-induced alterations may not be visible through simple observation but can significantly impact the accuracy, calibration, and functionality of dosimetry devices. For instance, reduced optical transmittance can affect laser alignment in water phantoms, while microstructural defects observed on material surfaces can reveal the onset of a mechanical failure. Chemical analysis can reveal degradation mechanisms whereas mechanical properties evaluation can detect dimensional changes that may cause misalignments, invalidating critical parameters in ICs such as calibration coefficients, quality correction factors, and ultimately, dose determination. Evaluating fragility is also important, as increased brittleness can lead to crack formation, potentially leaving the device unusable. Changes in electrical properties are particularly crucial for ICs, as significant variations in the permeability of non-conductive components can increase leakage current, while alterations in conductive components can compromise calibration coefficients.

This study aims to evaluate the structural and functional changes in various properties (optical, chemical, mechanical and electrical) of commonly used materials for QA device construction across a range of applications, under UHDR conditions. More detailed information on the materials studied and the typical use is provided in Table 4.1. This study specifically investigates how particle type (electrons and protons in this work), total deposited dose, and dose rate influence material degradation. By establishing the tolerances of these materials and identifying the most resistant materials to UHDR exposure, this work aims to provide recommendations for the selection of durable materials for QA device construction suited for UHDR radiotherapy applications.

4.2 Materials and methods

4.2.1 Materials

Two different sets of samples focused for different applications were used for this study, with their characteristics summarized in Table 4.1. Figure 4.2 provides an illustration of the two kinds of samples. The first set, referred to as Type ‘E’ (Electron-irradiated samples), is intended for studying thicker materials typically used in the manufacturing of water tanks and phantoms. The geometry selected is a rectangular prism of $10 \times 10 \text{ mm}^2$ surface with the following thicknesses and materials: 3, 5, 10, 15 and 20 mm *Polymethyl Methacrylate* (PMMA); 5 and 20 mm *Polyether ether ketone* (PEEK); 5 mm *Polycarbonate* (PC); 5 mm *Cyclic Olefin Copolymer* (TOPAS) and 4.8 mm *Clear Polystyrene* (CPS).

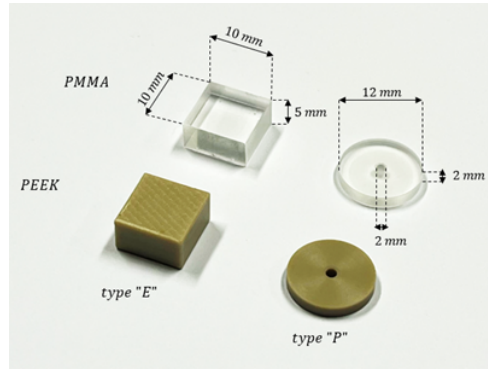


Figure 4.2: Example of Type ‘E’ sample with a $10 \times 10 \text{ mm}^2$ surface area and thickness of 5 mm of PMMA and PEEK. Type ‘P’ sample has an external diameter of 12 mm, an internal diameter of 2 mm and thickness of 2 mm.

The second set of samples, labeled Type ‘P’ (Proton-irradiated samples), focuses on studying thinner samples commonly used in the construction of ICs. While large recombination effects suggest that some ICs might not be suitable for UHDR electron beams [29], the dose rates achieved with protons are not as high [176], allowing ICs with smaller electrode spacing to be used under these circumstances even though recombination effects are still present [177]. Therefore, this set of samples was irradiated under proton beams. As recommended by international dosimetry protocols [78, 6], ICs with plane parallel geometry is preferred. Therefore, the chosen geometry is a disc with 2 mm inner diameter and 12 mm outer diameter with thickness of 0.5, 1, 1.5 and 2 mm. These dimensions are typical for ICs critical structures, such as the entrance window and collecting electrodes. The following materials are used for this set of samples:

PMMA; PEEK; *cross-linked polystyrene copolymer* (REXOLIT); *Polyoxymethylene* (POM); C-552 (or SCHONKA, air equivalent plastic); Graphite; Electrically Conductive POM (POM ELS) and Electrically Conductive PEEK (PEEK ELS).

Material	Colour	Conductive	Geometry	Thickness (mm)	Density (g/cm ³)
PMMA	Transparent	No	Type E	3, 5, 10, 15, 20	1.19
			Type P	0.5, 1, 1.5, 2	1.18
PEEK	Beige opaque	No	Type E	5, 10, 20	1.32
			Type P	0.5, 1, 1.5, 2	1.21
PC	Transparent	No	Type E	5	1.20
TOPAS	Transparent	No	Type E	5	1.01
CPS	Transparent	No	Type E	4.8	1.05
REXOLITE	Transparent	No	Type P	0.5, 1, 1.5, 2	1.05
POM	White	No	Type P	0.5, 1, 1.5, 2	1.41
C-552	Black	Yes	Type P	0.5, 1, 1.5, 2	1.76
GRAPHITE	Black	Yes	Type P	0.5, 1, 1.5, 2	2.26
POM ELS	Black	Yes	Type P	0.5, 1, 1.5, 2	1.41
PEEK ELS	Black	Yes	Type P	0.5, 1, 1.5, 2	1.36

Table 4.1: Materials and relevant characteristics of the samples used in this study.

The typical uses of the materials in this work include PMMA for water-tank walls, buildup caps, water-equivalent plates, phantoms, and IC components; PEEK, CPS, REXOLITE, C-552, POM ELS and PEEK ELS for IC components; PC and TOPAS for phantoms; POM for water-equivalent plates and IC buildup caps; and graphite for IC components and graphite calorimeter parts.

4.2.2 Experimental setup for irradiations

The electron irradiation was carried out with the dedicated research LINAC from the Metrological electron accelerator facility at PTB, Germany [27]. Type ‘E’ samples were irradiated with a 20 MeV electron beam, at a 10 Hz pulse repetition frequency and a pulse width of 2.5 μ s, inside a water tank at a Source to surface distance (SSD) of 50 cm. This resulted in a dose per pulse of about 10.5 Gy at the half-value depth (R50) [78] of 7.14 cm. All sets of samples were positioned at a depth of around 1 cm, to ensure the most uniform dose deposition through the sample. Samples were irradiated with six different dose levels: 10^2 , 10^3 , 10^4 , 10^5 , $5 \cdot 10^5$ and 10^6 Gy; the number of pulses delivered varied depending on the dose and dose per pulse selected in each experiment. One sample per condition was kept unirradiated. These conditions are labeled as experiment SSD50. For comparison

with other dose rates, an additional set of PMMA and PEEK samples were irradiated under two extra experiments: SSD70 and SSD50-C. Detailed characteristics of these experiments are provided in Table 4.2. The dose delivered to the samples was estimated using the in-beamline integrating current transformer, which was calibrated with a diamond detector [104] that had been previously calibrated against alanine dose measurements in a separate investigation [28]. Since this experiment does not need a high precision on the delivered dose, the uncertainty in the dose estimation in the QA was large, around 5%.

Experiment	Energy (MeV)	Collimator	FWHM at Z_{ref} (mm)	SSD (cm)	Z_{ref} (mm)	t_{puls} (μs)	f_{puls} (Hz)
SSD70	20	None	79.9	70	46.2	2.5	5
SSD50-C	20	$\phi = 5$ cm	49.7	50	41.2	2.5	10
SSD50	20	Nose	47.3	50	41.9	2.5	10

Experiment	DPP (Gy)	$\dot{D}_{\text{inst}}$ (Gy/s)	$\dot{D}_{\text{av}}$ (Gy/s)	D (Gy)
SSD70	6.5	$2.6 \cdot 10^6$	32.4	0, 10^2 , 10^3 , 10^4 , 10^5 , $5 \cdot 10^5$ and 10^6
SSD50-C	11.5	$4.6 \cdot 10^6$	115	0, 10^2 , 10^3 , 10^4 , 10^5 , $5 \cdot 10^5$ and 10^6
SSD50	10.5	$4.2 \cdot 10^6$	105	0, 10^2 , 10^3 , 10^4 , 10^5 , $5 \cdot 10^5$ and 10^6

Table 4.2: Experiment specifications for the electron (e) irradiations.

We want to emphasize that particular care was taken to ensure dose homogeneity in order to minimize localized effects which could influence the measured properties. Collimators were used to shape the beam, ensuring a sufficiently large, flat, and homogeneous irradiation field (e.g. for SSD70, flatness was 1% over 10 mm, and dose uniformity in depth was within 5% over 2 cm). To minimize dose gradients with depth during electron irradiations, samples were placed side-by-side rather than stacked. Proton irradiations were conducted with samples stacked in the plateau region, where dose uniformity with depth was ensured. Sample positions were marked and tracked to ensure no differences were found across the entire sample. Measurements were taken across different surface locations, and for macroscopic tests, different sample orientations were used. These checks consistently confirmed the uniformity of irradiation and the reproducibility of the material response across different parts of the sample.

Type ‘P’ samples were irradiated in air with a 68 MeV broad pulsed proton beam with the pulsing chopper-based system of the Arronax C70XP cyclotron [152] at Arronax, France. The different dose levels and dose rates achieved are summarized in Table 4.3. To achieve the 4×4 cm² field size, the beam was spread with a 300 μm tungsten target placed in the beamline, which resulted in an effective

energy to the samples about 64 MeV, and collimated with paraffin blocks. For the $1 \times 1 \text{ cm}^2$ field size, no target or collimator were added. The estimation of the average dose delivered to the samples in this setup was done using films [186] for the profiles as the beam was not homogeneous. To estimate the dose, a Faraday cup was used to measure the cumulated dose and cross-calibrated against an IC at low dose rates where recombination losses can be corrected [163, 39].

Experiment	Energy (MeV)	Field size (cm ²)	t_{puls} (ms)	T (ms)	$\dot{D}_{\text{inst}}$ (Gy/s)	$\dot{D}_{\text{av}}$ (Gy/s)	D (MGy)	t_{total} (h)
P1	68	4x4	0.05	1.8	$9.0 \cdot 10^3$	141	0.42	0.8
P2	68	4x4	1	21	$2.1 \cdot 10^3$	105	1.02	2.7
P3	68	1x1	1	41	$8.4 \cdot 10^3$	216	1.09	1.4
P4	68	1x1	1	5	$2.6 \cdot 10^3$	500	1.00	0.6

Table 4.3: Experiment specifications for the proton (p) irradiations. P0 would be the pristine, non-irradiated, samples.

4.2.3 Sample characterization

Optical properties

A *UV-VIS-NIR Spectrophotometer UV-3600 Plus* from *Shimadzu* was used to quantify color changes in the irradiated samples, by measuring changes in transmittance relative to the non-irradiated samples, as radiation-induced optical changes can affect transparency which is directly related to material damage and chemical changes. The transmittance spectrum was recorded across wavelengths ranging from 200 to 800 nm, with a resolution of 0.5 nm. Spectra were normalized at the lowest wavelength, and values were compared at 420 nm [46] as this wavelength is typically related to the yellowness of the sample evaluate which is the typical change observed in plastic degradation. To enhance the signal-to-noise ratio and improve the readings accuracy, two measurements modes were used based on transparency. For highly transparent samples, transmittance mode was used. For non-transparent samples, measurements were conducted in absorbance mode and latter converted to transmittance using known relations.

Scanning electron microscopy (SEM) analysis was used to investigate the surface morphology of the samples to investigate primary signs of structural degradation such as micro-cracks or micropores formation due to gas release [56]. This technique is particularly well-suited for electrically conductive materials, where surface details can be accurately assessed without additional preparation. Although the main focus of the SEM analysis was on conductive samples, non-conductive samples were also examined as an exploratory step. Non-conductive samples were

imaged without applying conductive coatings in this study to avoid altering their native surface. This approach is essential to preserve the possibility of repeat the measurements and long-term follow-up on potential permanent damage or material recovery, without compromising the original material properties.

Irradiation might induce changes in the electrical conductivity of some materials initially classified as non-conductive. By comparing irradiated and non-irradiated samples with SEM analysis, we aimed to assess whether any visible surface changes could indirectly indicate such conductivity shifts as suggested in [56], particularly in relation to the dielectric constant variations observed in the electrical properties' analysis.

A JEOL JSM—7100F Field Emission Scanning Electron Microscope was used under ultra-high vacuum conditions, employing accelerating voltages of 2, 5 and 15 kV and magnifications of x20, x200, x900 and x1600.

Chemical properties

To investigate chemical and molecular changes in the sample structure as chemical degradation may occur even in the absence of visible damage or changes in bulk physical properties, fourier transform infrared (FTIR) spectroscopy was performed using a *Nicolet iN10 Infrared Microscope* equipped with a mercury cadmium telluride in attenuated total reflectance mode. Spectra were measured across a range of $675\text{--}4000\text{ cm}^{-1}$ with a resolution of 2 cm^{-1} , averaging 64 scans per sample to ensure a high signal-to-noise ratio. Background spectra were acquired and subtracted from each measurement. Standard pressure was applied to samples during collection, and the detector was cooled with liquid nitrogen to enhance sensitivity. After acquisition, all spectra were baseline-corrected, normalized, and analyzed using *Omnic Spectra* software from *Thermo Fisher Scientific Inc.*

Due to the specific relevance of graphite in ionization chamber construction (e.g. for collecting electrodes or walls in cylindrical ICs) and its use in other detectors such as graphite calorimeters, additional characterization of graphite samples was performed using Raman spectroscopy as FTIR is not suitable for graphite characterization due to its highly ordered structure and lack of infrared-active functional groups [62]. A *Reinshaw Qontor inVia Raman microscope* was employed. The Raman spectra were acquired using a 785 nm laser, with measurements taken at multiple points across the sample surface. Acquisition parameters included an exposure time of 15 s, laser power set to 10%, and a total of 3 accumulations, with a Raman shift range of $827\text{--}1896\text{ cm}^{-1}$. Automatic baseline correction was applied to all spectra, and the intensity of the G and D bands was analyzed.

Mechanical properties

To evaluate the potential impact of UHDR irradiation on the structural integrity of the materials, we assessed several key mechanical properties that could be affected by radiation-induced degradation. Specifically, we studied dimensional stability, hardness, and fragility, as these properties are critical for ensuring the long-term functionality and mechanical reliability of QA devices. A Palmer micrometer with a 1 μm resolution was used to identify possible changes in dimensions of the different samples. Hardness was evaluated via micro-indentation with the *Micro indenter EMCO Durascan 70G5* equipped with a Vickers tip. A quasi-static load function with a peak force ranging 0.05–1 N was applied. A minimum of 10 indentations were performed through the surface. Fragility was evaluated indirectly by observing the presence or absence of rifts around the indentation marks left by the hardness tests.

Electrical properties

The conductivity and dielectric constant of the samples to evaluate permanent changes in these electric properties were measured using a *Novocontrol alpha high resolution impedance/dielectric Analyzer*. Measurements were conducted at a fixed alternating current (AC) voltage of 1 V, across a frequency range of 10^3 – 10^7 Hz of the applied AC voltage signal. All components of the complex dielectric permittivity, the loss tangent, phase angle, conductivity and impedance components were determined as a function of the frequency, however only changes on the real part of permittivity (ϵ), and conductivity were analyzed and reported in this work. Since the measured values of ϵ are highly dependent on the conditions under which the measurements are performed, all samples were analyzed on the same day and measurements were repeated across several days. ϵ values for comparison were taken at 100 Hz to mitigate the effects of capacitance dependence at higher frequencies, as described by [69]. The relative change in ϵ with respect to non-irradiated samples was used for comparative analysis.

4.3 Results

Figures 4.3 and 4.4 show the external appearance of the different samples irradiated with electrons and protons. For PMMA type 'E' samples, the gradual change in color with increasing dose levels is clearly visible (Figure 4.3 (a)). It can also be observed that optical density recovers over time (Figure 4.3 (b))—two years post-irradiation (Y2), when compared to the appearance shortly after irradiation (Figure 4.3 (a))—Y0), which aligns with trends described in the literature [41].

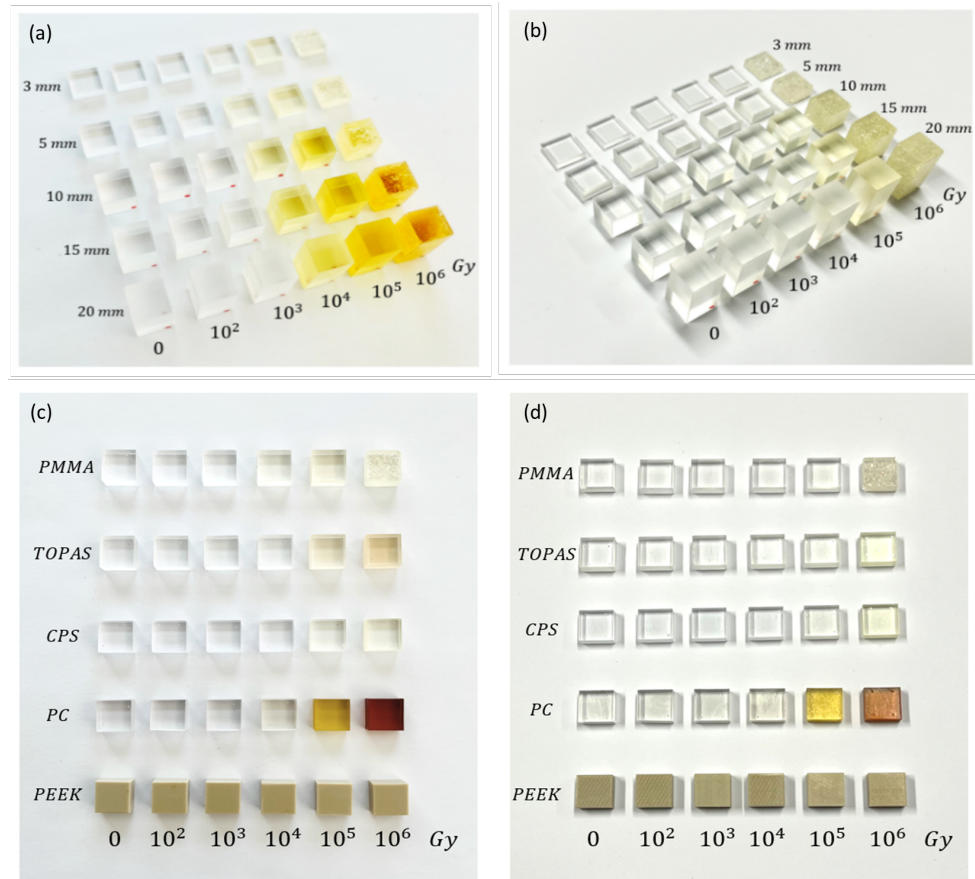


Figure 4.3: External appearance of type 'E', electron irradiated samples in experiment SSD50. (a) PMMA samples of different thickness and dose levels. (b) Same samples as (a) two years later. (c) Different materials with 5 mm thickness and dose levels. (d) Same samples as (c) two years later.

In general, gradual color changes were observed for all transparent materials (Figures 4.3 (c) and 4.4). Significant opacification occurred for PC samples starting at dose levels around 10⁵ Gy for electron irradiation. Black materials maintained their color with no noticeable change (Figure 4.4), except for POM ELS, which seemed to lose its shiny appearance, turning its surface matt. PEEK samples showed a slight color shift towards warmer tones when irradiated with 10⁶ Gy, regardless of particle type which did not recover over time (Two years later, Figure 4.3 (d)). Both PMMA (observed in both particle types (see Figures 4.3 (a) and 4.4) and POM (see Figure 4.4) exhibited significant radiation induced

stress fractures. While PMMA retained its structural integrity, POM samples were completely destroyed.

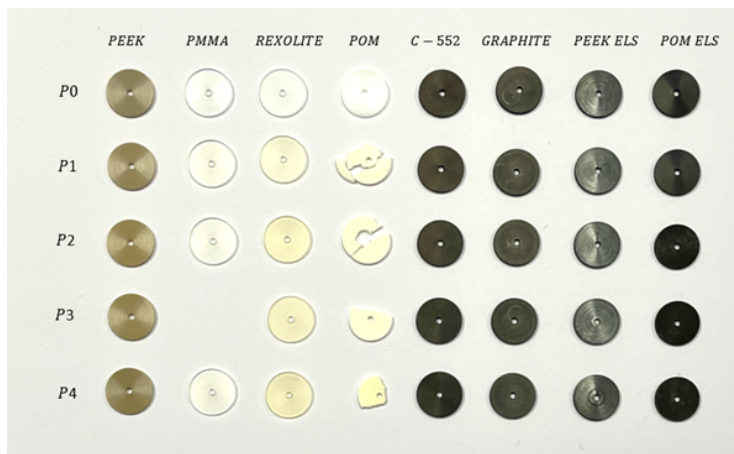


Figure 4.4: External appearance of type 'P' samples; pristine (P0) and irradiated with proton beams under different conditions (P1–P4).

4.3.1 Optical properties

UV–Vis analysis of PMMA indicated a decrease in transmittance spectra as the radiation dose increased (Figure 4.5 (a)). This decrease correlates with the observed yellowing of the samples, likely attributed to the introduction of conjugated carbonyl groups in the polymer chain [46]. A partial recovery in color was observed two years post-irradiation, with UV–Vis analysis revealing up to a 30% increase in transmittance for thicker samples (>5 mm) and a 5–10% increase for thinner samples (≤ 5 mm).

Figure 4.5 (b) highlights the dependence of transmittance on sample thickness for PMMA. Figures 4.5 (c) and (d) show the transmittance at 420 nm for type 'E' and 'P' samples, respectively, for various materials. For PMMA type 'E' samples, no significant differences in transmittance were observed between different dose rates (Figure 4.5 (e)). Conversely, type 'P' samples exhibited differences in transmittance; however, these differences did not show a clear correlation with dose rates.

When comparing the effects of different particle types, it is clear that no fair comparison can be made due to the dependence of the transmittance with the sample thickness. Figure 4.5 (f) illustrates this dependency for type 'E' and 'P' PMMA samples irradiated with 1 MGy, showing a continuous trend across both sets.

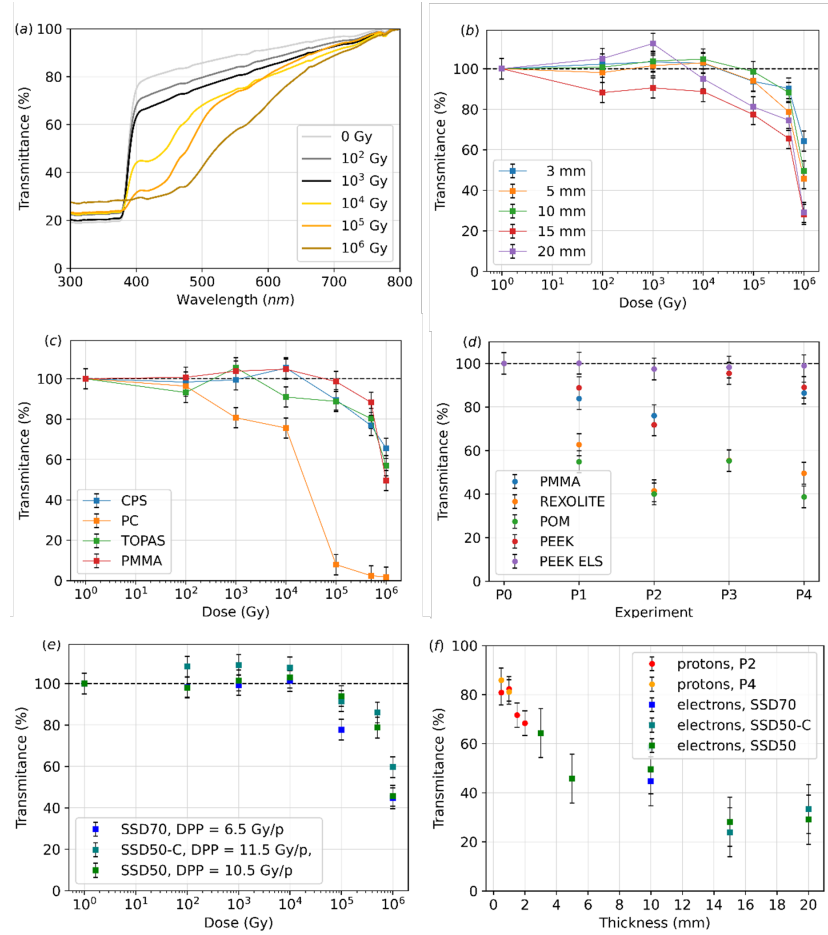


Figure 4.5: Results for the UV-Vis spectroscopy. (a) Example of the transmittance spectra versus the wavelength for the different dose levels (presented in different shades of yellow line colors) for the 3 mm PMMA type 'E', electron irradiated samples. (b) Transmittance of type 'E' PMMA samples of different thicknesses (presented in different line colors) irradiated with electrons in experiment SSD50 for different dose levels. (c) Transmittance comparison of type 'E' different materials (presented in different line colors) from experiment SSD50 for different dose levels. (d) Transmittance comparison of type 'P', proton irradiated materials (presented in different colored points) for the 0.5 mm samples on different experiments. (e) Transmittance for different dose levels for type 'E' PMMA samples irradiated in the three different experiments (presented in different colored points) performed at different dose rates. (f) Transmittance for different thickness of PMMA samples irradiated with 1 MGy protons (presented in red and orange points) and electrons (presented in green and different shades of blue points) in different experiments.

SEM analysis on conductive samples (Figure 4.6 (a)) revealed no observable differences in the surface of PEEK ELS and C-552 samples across the different irradiation conditions. For graphite samples, smoother and larger surface chunks were identified in irradiated sets compared to non-irradiated samples. These changes, did not exhibit significant variation between different experimental conditions, suggesting limited dependence on dose or dose rate.

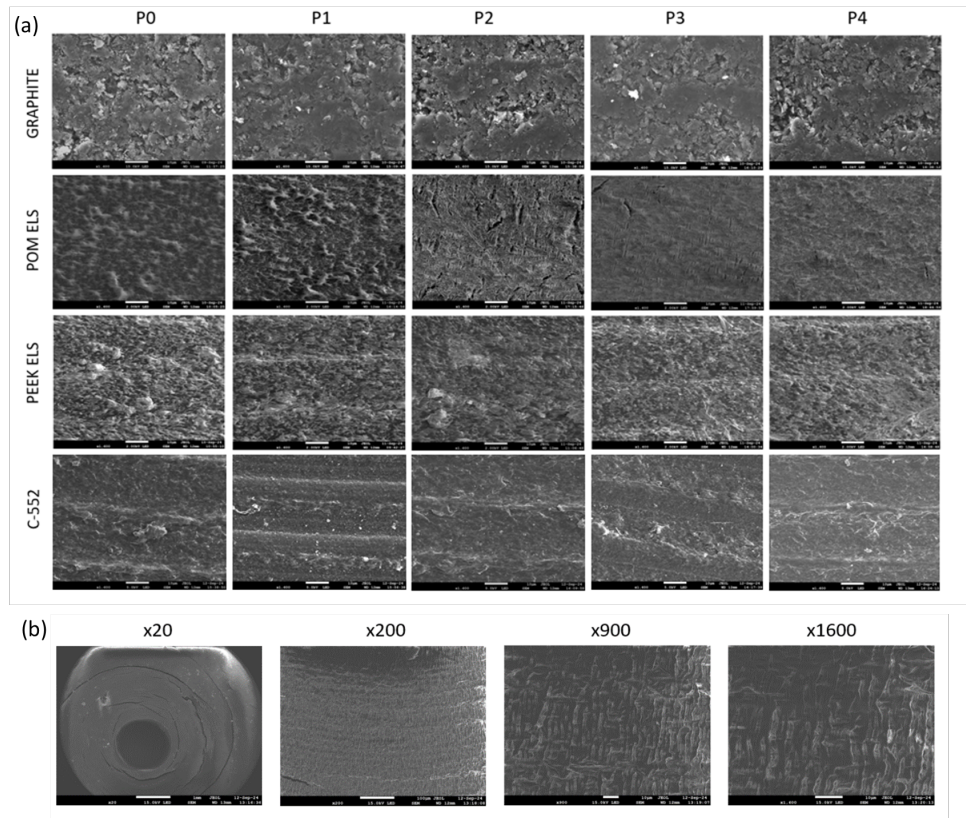


Figure 4.6: (a) SEM visualization of surface of 1 mm type 'P', proton irradiated samples of different conductive materials, at x1600, accelerating voltage of 15 kV from pristine samples (P0) and all consecutive experiments with protons (P1, P2, P3 & P4). (b) SEM visualization of surface of POM samples for different augmentations from experiment P4.

Significant changes were found in the surface of POM ELS samples. Multiple rifts and surface fissures were evident, with the greatest density and size of rifts appearing in samples irradiated in experiment P2. This was followed by experiments P3 and P4, with progressively fewer rifts observed. However, no clear correlation was found between the observed changes and the dose rate.

Although SEM is not typically suitable for analyzing non-conductive samples, irradiated POM samples could be successfully analyzed, indicating an increase in surface conductivity induced by irradiation. This finding aligns with the electrical characterization results in section 4.3.4. Figure 4.6 (b) shows detailed SEM images of irradiated POM samples at different magnifications (x20, x200, x900, and x1600), highlighting the presence of rift-like patterns across the surface. These microstructures are consistent with the degradation seen in POM ELS samples and may be attributed to gas release during irradiation which leads to surface cracking, as reported in previous studies [56].

4.3.2 Chemical properties

The FTIR spectra of various materials are presented in Figures 4.7-4.10. This analysis focuses on the observed spectral changes, as a comprehensive discussion of all peaks is beyond this study's scope. Overall, the obtained spectra align well with their expected profiles.

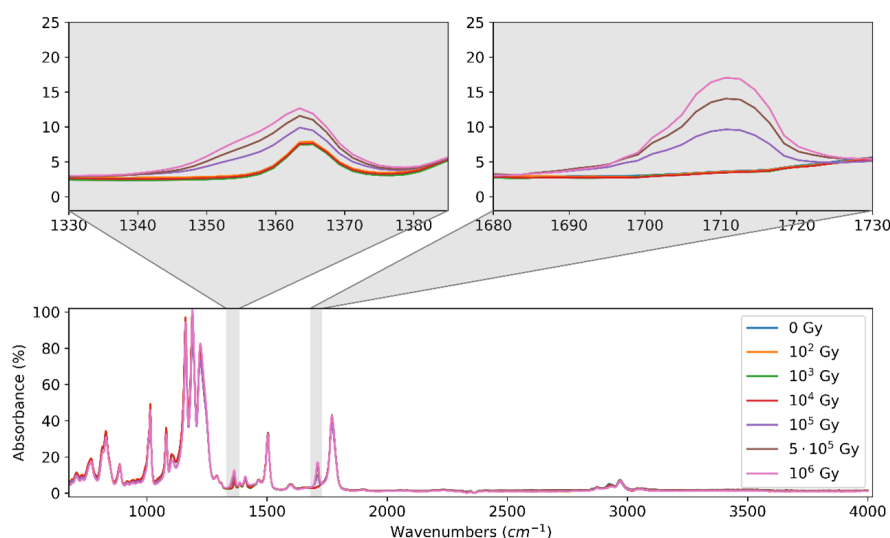


Figure 4.7: FTIR spectra of PC for different dose levels (different line colors) studied in experiment SSD50 of electron irradiated samples analyzed two years after the irradiation was performed. Zoom-in of the relevant parts of the spectra that displayed changes are presented.

FTIR analysis revealed no significant changes in the spectra of CPS, PEEK, REXOLITE and PEEK ELS spectra. For the remaining materials, FTIR analysis demonstrated that radiation-induced oxidative degradation, particularly the formation of carbonyl groups around 1720 cm^{-1} , was a common mechanism across

all polymers [34]. Specific spectral changes, varied depending on the material and dose level, with some evidence of partial recovery over time in certain cases. Specifically, C-552 showed a gradual, slight increase in absorbance around 1720 cm^{-1} and 2930 cm^{-1} with increasing dose levels, attributed to the formation of carbonyl groups and oxidation processes.

For PC electron irradiated samples, no changes were observed in the initial FTIR analysis (Y0). However, after two years (Y2), subtle modifications were detected, as shown in Figure 4.7, with slight peak shifts and changes in peak intensity with dose levels starting at 10^5 Gy . In the region $1330\text{--}1380\text{ cm}^{-1}$, a gradual increase in absorbance was observed. The carbonyl group region ($1700\text{--}1720\text{ cm}^{-1}$) exhibited similar behavior, further confirming radiation-induced oxidative degradation [70].

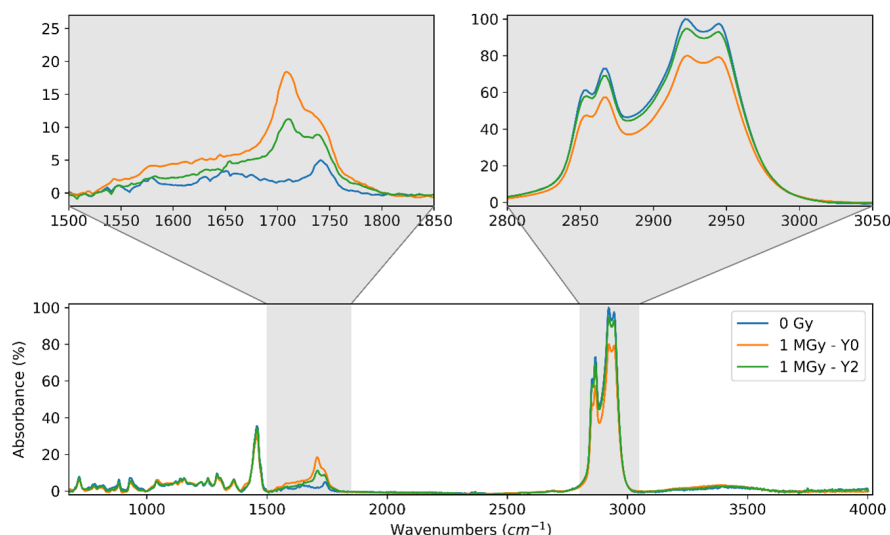


Figure 4.8: FTIR spectra of TOPAS irradiated with electrons. Comparison between non-irradiated sample (Blue line, 0 Gy); irradiated sample with 1 MGy performed shortly after the experiment SSD50 (Orange line, 1 MGy—Y0); and the same 1 MGy irradiated sample analyzed again two years later (Green line, 1 MGy—Y2). Partial recovery of the sample absorbance is observed, as the Y2 spectrum tends to revert towards the shape of the non-irradiated spectrum.

TOPAS also showed dose-dependent changes, particularly an increase in absorbance around 1700 cm^{-1} , again associated with carbonyl group formation. In addition, a decrease in absorbance in the $2800\text{--}3000\text{ cm}^{-1}$ region was observed, reflecting possible C-H group modifications such as chain scission and cross-linking [168]). Analysis performed two years later revealed partial recovery, with a reduction in oxidation products in the carbonyl region ($1500\text{--}1850\text{ cm}^{-1}$) and an

increase in absorbance in the C-H stretching region ($2800\text{--}3050\text{ cm}^{-1}$), indicating polymer chain reorganization and stabilization. Overall, while radiation damage was evident, some structural changes appeared to recover over time (see Figure 4.8).

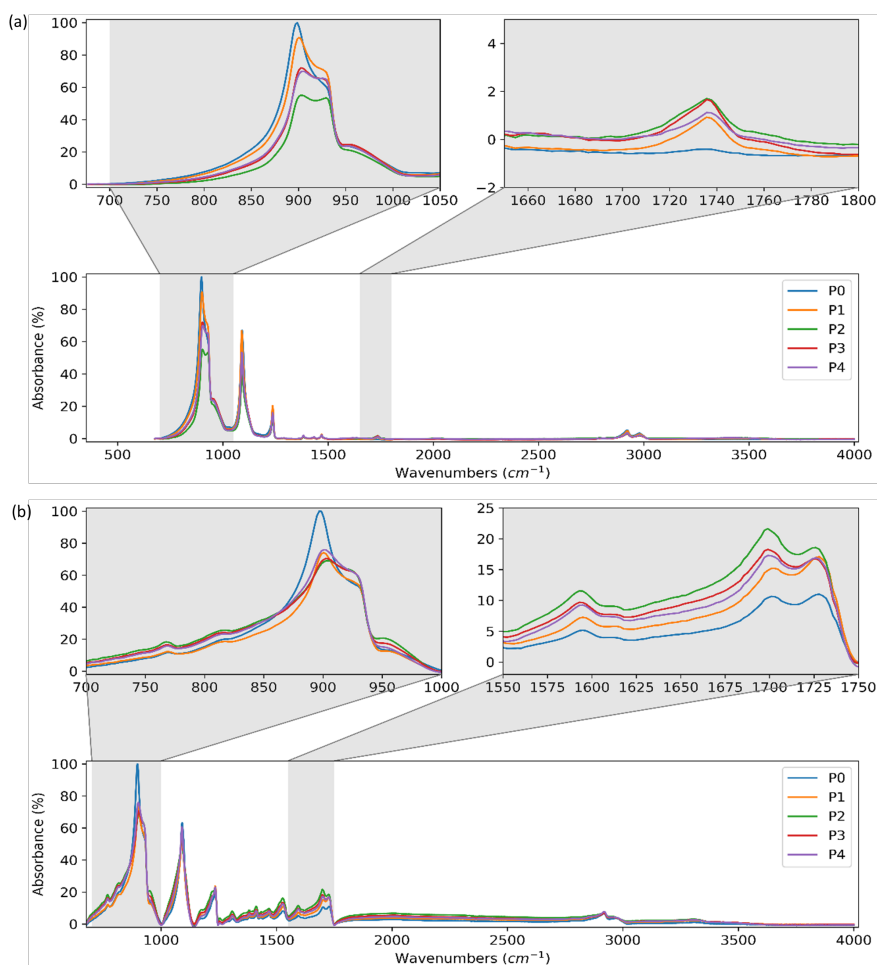


Figure 4.9: FTIR spectra of POM (a) and POM ELS (b) irradiated with protons (different line colors). Zoom-in of the relevant parts of the spectra that displayed changes are presented.

POM exhibited a decrease in absorbance around 900 cm^{-1} , where characteristic C–O and C–H bonds appear. This decrease is attributed to oxidation and cross-linking, which disrupt these bonds. Additionally, an increase in absorbance in the $1700\text{--}1780\text{ cm}^{-1}$ region confirmed the presence of carbonyl groups from oxidative degradation [184]. Among the experiments, the most significant differences were

observed in P2, with progressively fewer changes in P3 and P4, and the smallest differences in P1, consistent with the lower radiation dose (see Figure 4.9 (a)).

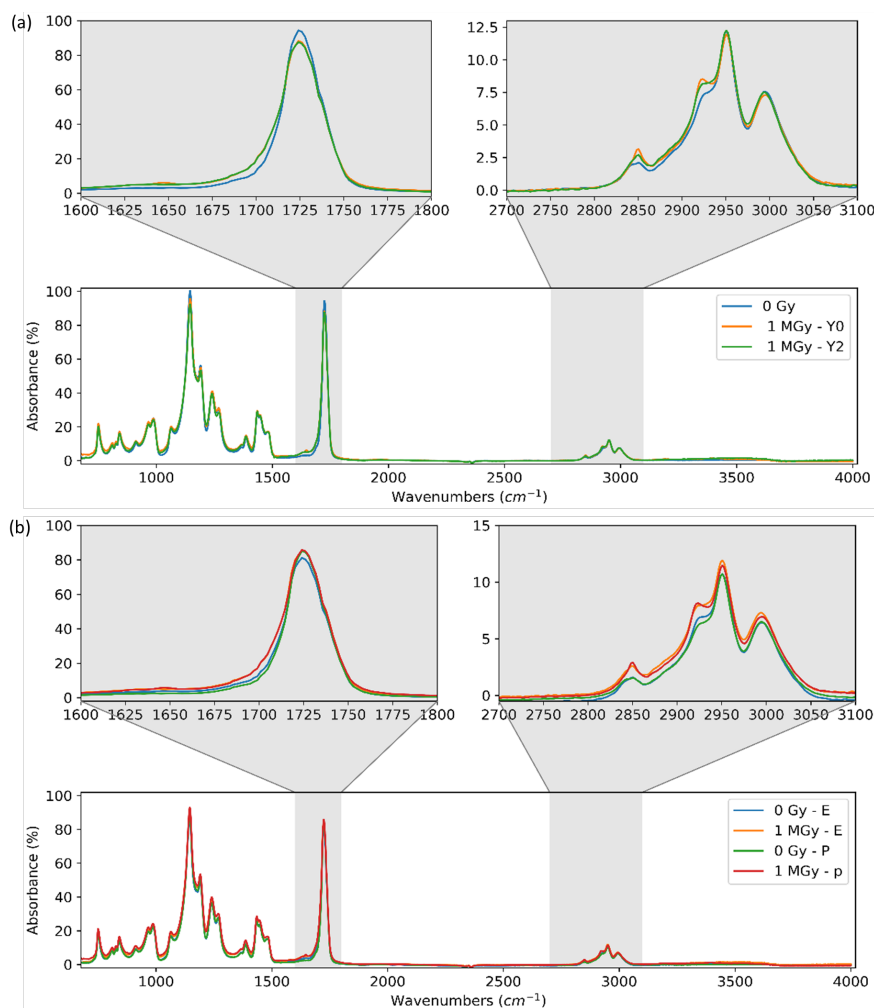


Figure 4.10: FTIR spectra of PMMA. (a) Comparison of absorbance spectra of electron irradiated samples between non-irradiated sample (Blue line, 0 Gy) first FTIR (Orange line, 1 MGy—Y0) and secondary analysis performed two years later (Green line, 1 MGy—Y2). (b) Comparison of absorbance spectra between non-irradiated type-E sample (Blue line, 0 Gy—E), 1 MGy electron irradiated sample in SSD50 experiment (Orange line, 1 MGy—E), pristine type-P sample (Green line, 0 Gy—P) and 1 MGy proton irradiated sample in P2 experiment (Red line, 1 MGy—p).

Similarly, POM ELS showed a decrease in absorbance and peak broadening around 900 cm^{-1} , linked to oxidation and chain scission affecting C–O vibrational modes [109]. The carbonyl region ($1550\text{--}1750\text{ cm}^{-1}$) exhibited an increase in absorbance, further confirming oxidative degradation. The progression of changes across different dose levels mirrored that observed in POM (Figure 4.9 (b)).

PMMA showed some differences between the initial analysis (Y0) and the follow-up conducted two years later (Y2) as shown in Figure 4.10 (a), where the spectra highlight changes in both carbonyl (1720 cm^{-1}) and C–H regions ($2800\text{--}3100\text{ cm}^{-1}$) linked to oxidative degradation. A slight recovery of the material was observed. A comparison between electron and proton irradiation (Figure 4.10 (b)) revealed similar impact on the material, which was expected given the comparable LET of both particles under the investigated conditions [46].

Representative Raman spectra of graphite samples irradiated with protons are presented on Figure 4.11 (a) for the different conditions. The characteristic D band of graphite, observed around 1309 cm^{-1} , is associated with structural defects and disorder, while the G band around 1578 cm^{-1} corresponds to the stretching vibrations of sp^2 carbon-carbon bonds in the graphite lattice. Additionally, the D' band near 1605 cm^{-1} is related to further disorder in the graphitic structure. While the spectra are consistent with the expected vibrational modes of graphite [36], the irregular surface morphology of the samples introduced significant statistical noise in the measurements. Despite this noise, no significant differences in the Raman spectra were identified across the experimental conditions.

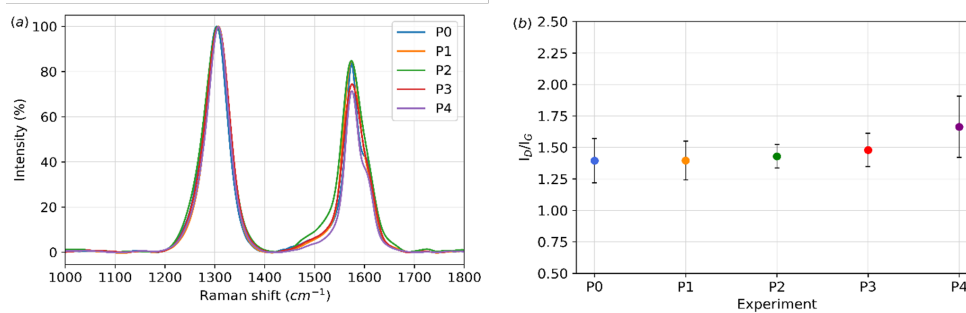


Figure 4.11: (a) Representative Raman spectra of graphite for the different experiments with protons presented in different line colors). (b) Intensity ratio between D and G bands for different experiments (presented in different scattered point colors).

Figure 4.11 (b) shows the intensity ratio between D and G bands, which offers information about possible structural disorder or defects. The Raman spectrum

and ratio remained almost constant across all experimental conditions, with variations falling within the uncertainty range.

4.3.3 Mechanical properties

Type 'E' samples exhibited large manufacturing tolerances, and no measurable changes in dimensions were observed after irradiation. In contrast, Type 'P' samples were fabricated with standard tolerances typically used for ICs construction (around 0.5%). Figure 4.12 shows the relative changes in thickness and diameter averaged for the different materials and experimental conditions for type 'P' samples. It can be clearly seen that POM and its conductive version, POM ELS exhibited significant dimensional reductions in both thickness and diameter.

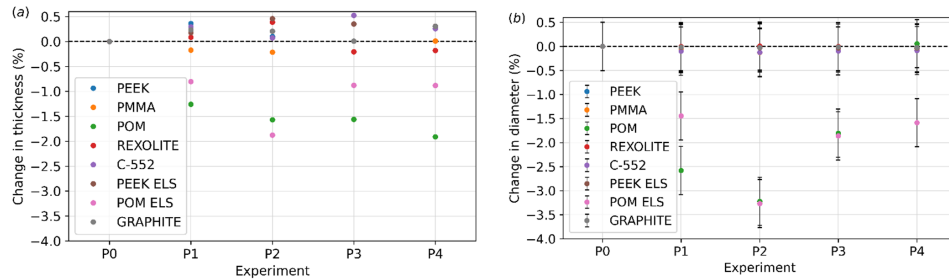


Figure 4.12: (a) Change in thickness for type 'P', proton irradiated samples in different experiments (P0, P1, P2, P3 and P4) of different materials (presented in different scattered point colors). Values were averaged for all thicknesses and normalized at the nominal value of the pristine samples. To enhance clarity no error bars were displayed. Typical type-A error was found around 0.5%. (b) Same graph but representing the relative change in diameter.

Figure 4.13 (a) presents the results of micro-indentation tests performed on Type 'P' samples. POM irradiated samples fractured during testing, indicating significant material embrittlement. POM ELS showed a significant reduction in hardness, with similar results observed across experiments P2, P3, and P4, corresponding to approximate dose levels of 1 MGy. For Type 'E' samples, the results are shown in Figure 4.13 (b). PMMA demonstrated a significant decrease in hardness with increasing dose levels. The hardness of TOPAS exhibited only a slight reduction with dose, while other materials showed no significant changes. Figure 4.13 (c) compares the hardness of PMMA Type 'E' samples across different experiments and dose rates. The results indicate no measurable differences between the different dose rates. Furthermore, no change in hardness was observed when tests were repeated two years after irradiation (Y2) compared to the initial post-

irradiation tests (Y0), suggesting that the reduction in hardness is permanent, with no recovery over time. Figure 4.13 (d) provides a comparative analysis of PMMA Type 'E' and Type 'P' samples across different dose levels. Type 'P' samples did not exhibit a decrease in hardness with dose levels, unlike Type 'E' samples. This discrepancy may be attributed to substrate effects masking potential changes in the material.

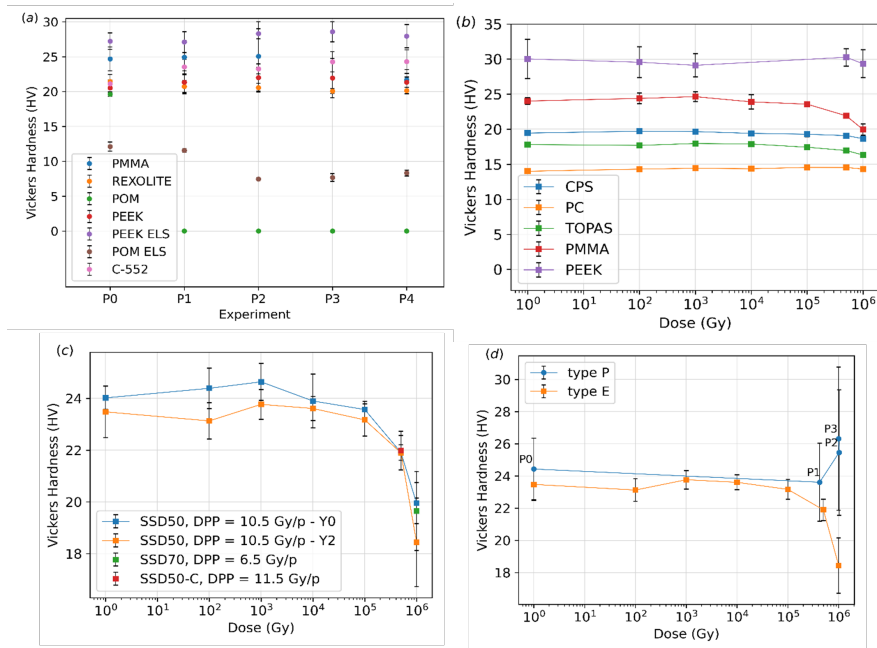


Figure 4.13: (a) Hardness tests results for the type 'P' proton irradiated samples in different experiments (P0, P1, P2, P3 and P4) for different materials (presented in different scattered point colors). (b) Hardness values for type 'E' electron irradiated samples of different materials (presented in different line colors) for different dose levels in experiment SSD50. (c) Hardness for type 'E' PMMA samples for the three different experiments (SSD50, SSD70 and SSD50-C) performed at different dose rates. Results for SSD50 experiment are displayed for the analysis performed shortly after irradiation (Blue line with scattered points, Y0) and two years later (Orange line with scattered points, Y2). Result for SSD70 experiment is displayed in the green scattered point. Result for SSD50-C experiment is displayed in the red scattered point. (d) Comparison of type 'E' and 'P' PMMA samples hardness. The orange line with scattered points represents the results for SSD50 experiment with electrons. The blue line with scattered points represents the results for the experiments with protons. Each point is labeled with the corresponding experiment (P0, P1, P2, P3).

During micro-indentation, formation of rifts around the indent were observed for some irradiated materials exposed to a dose of 1 MGy. Non-irradiated samples did not exhibit this rift formation, indicating an increase in sample fragility as a result of irradiation. This phenomenon was observed for PMMA (see Figure 4.14), independently of the particle type, and in other materials such as PC, TOPAS, POM and POM ELS.

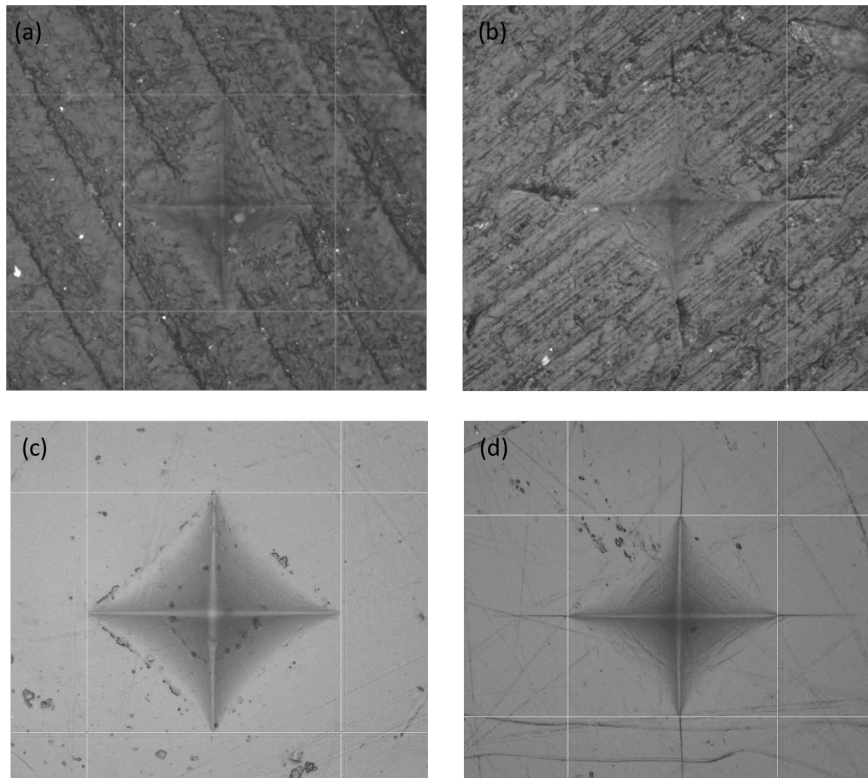


Figure 4.14: (a) 1 mm PMMA indentation marks of non-irradiated type 'P' samples. (b) Irradiated type 'P', proton irradiated samples from experiment P4. (c) 3 mm type 'E' non-irradiated samples. (d) Electron irradiated type 'E' samples with 1 MGy from experiment SSD50. It can be seen how the pressure from the indenter caused stress fractures around the diagonals, indicating a significant increase in fragility.

4.3.4 Electrical properties

Figure 4.15 (a) presents the dielectric constant (ϵ) of type 'E' PMMA samples irradiated at various dose levels as a function of frequency. Figure 4.15 (b)

illustrates the relative change in dielectric constant for various materials in type 'E' samples. For samples of varying thickness, results were averaged across all thicknesses. No significant differences were observed across different dose levels, except in the case of PMMA, which exhibited a gradual increase in the dielectric constant of up to 7% starting at dose levels of 10^5 Gy. This increase was found to be independent of sample thickness.

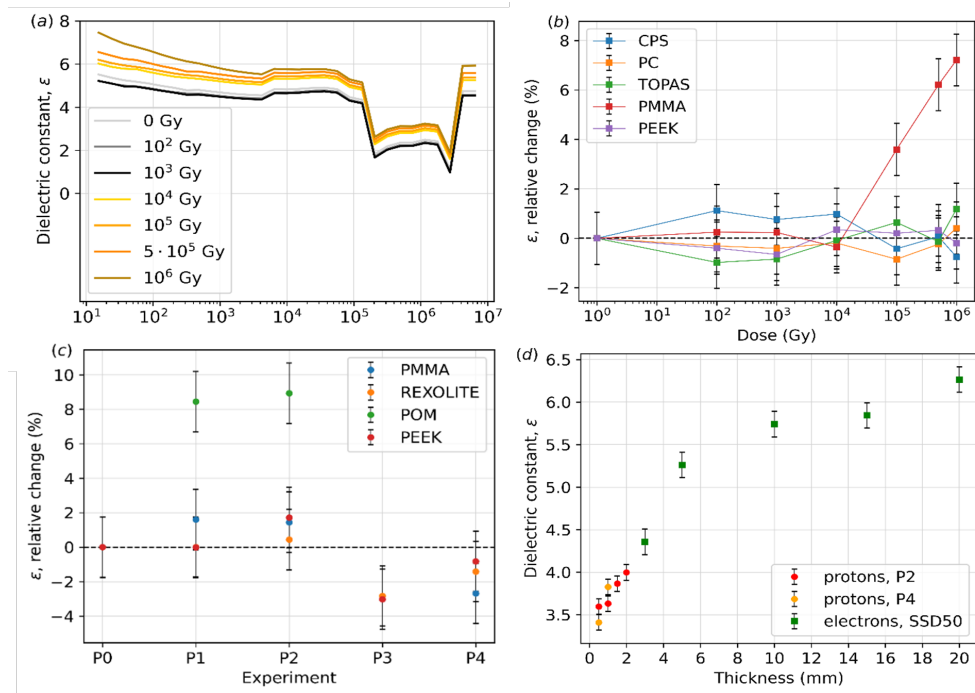


Figure 4.15: (a) Dielectric constant of PMMA for 3 mm type 'E', electron irradiated samples from experiment SSD50 as a function of frequency of the applied AC voltage signal for different dose levels (presented in different shades of yellow line colors). (b) Dielectric constant for type 'E' samples of different materials (presented in different colors of lines with scattered points) at different dose levels from experiment SSD50. (c) Dielectric constant for type 'P', proton irradiated samples of different materials (presented in different colors of scattered points) for different experiments (P0, P1, P2, P3 and P4). (d) Comparison dielectric constant of PMMA for different thickness of samples irradiated with protons (presented in red and orange points, which correspond to experiment P2 and P4, respectively) and electrons (presented in green points, corresponding to experiment SSD50).

Similarly, Figure 4.15 (c) displays the relative change in dielectric constant for type 'P' samples. Among these, only the dielectric constant of POM exhibited a

notable change. Results for experiments P3 and P4 are not included due to the complete fragilization of samples during handling. Figure 4.15 (d) highlights the dependence of the PMMA dielectric constant on sample thickness under different irradiation conditions. This observed variation in dielectric constant with thickness aligns with prior findings reported by [69].

As discussed in section 4.3.1, a fair comparison between particle types cannot be made due to the intrinsic dependence of the dielectric constant on sample thickness. Nevertheless, a continuous trend is evident across both sets of samples. Furthermore, no change in the dielectric constant was observed in samples analyzed shortly after irradiation (Y0) or two years post-irradiation (Y2), indicating that the changes in this property did not vary over time.

Figure 4.16 (a) presents graphite conductivity as a function of frequency. For relative comparison, conductivity values were taken at 1 MHz. Figure 4.16 (b) shows conductivity for various materials across different experiments with protons. It can be seen a significant change in conductivity for POM ELS samples. The largest relative change, compared to the non-irradiated condition (P0), was observed in experiment P2. Subsequent experiments, P3, P4, and P1, demonstrated progressively smaller relative changes. In contrast, the rest of materials did not exhibit any significant changes in conductivity.

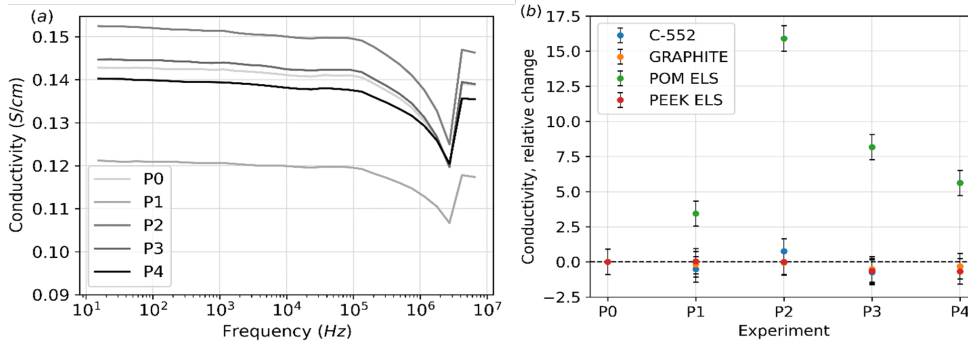


Figure 4.16: (a) Conductivity of graphite as a function of frequency of the applied AC voltage signal for different proton experiments (P0, P1, P2, P3 and P4, represented in different shades of grey). (b) Relative change of conductivity for the different experiments with protons (P0, P1, P2, P3 and P4) with different conductive materials (represented in scattered points of different colors).

4.4 Discussion

Table 4.4 provides an overview of the outcomes of the various tests conducted on different materials and sample types. The results indicate that radiation damage effects vary greatly depending on the material. In the following paragraphs, an overview of the most concerning changes in each of the materials is provided, clarifying what determines their suitability or not for UHDR applications.

Material	Sample type	Properties								
		Optical		Chemical		Mechanical			Electrical	
		UV-VIS	SEM	FTIR	Raman	Dimensions	Hardness	Fragility	ϵ	Conductivity
PMMA	E	x	-	x	-	-	x	x	x	-
	P	x	-	x	-	ok	ok	x	ok	-
PEEK	E	-	-	ok	-	-	ok	ok	ok	-
	P	ok	-	ok	-	ok	ok	ok	ok	-
PC	E	x	-	x	-	-	ok	x	ok	-
TOPAS	E	~	-	x	-	-	~	x	ok	-
CPS	E	~	-	ok	-	-	ok	ok	ok	-
REXOLITE	P	~	-	ok	-	ok	ok	ok	ok	-
POM	P	x	-	x	-	x	x	x	x	-
C-552	P	-	ok	~	-	ok	~	ok	-	ok
GRAPHITE	P	-	~	-	ok	ok	-	ok	-	ok
POM ELS	P	-	x	x	-	x	x	x	-	x
PEEK ELS	P	ok	ok	ok	-	ok	ok	ok	-	ok

Table 4.4: Resume of the results of the different tests performed. ‘x’ indicates crucial or very significant characteristics were altered in the sample. ‘ok’ indicates no observable differences were found. ‘~’ indicates small differences were found. ‘-’ indicates test was not performed in that sample. Please note that Fragility was not measured directly, observed phenomena of cracks during Vickers indentation test provided information about material's brittleness.

PMMA, POM, and its conductive variant (POM ELS) are strongly discouraged for use in UHDR conditions due to significant degradation found in most properties, specially brittleness that compromised its structural integrity. This issue is evident in the ICs and the top-right water phantom images from Figure 4.1, all made of PMMA (note that the bottom-left IC is covered by a thin layer of black lacquer). PC is also not recommended; multiple properties varied and the loss of transparency makes it impractical for see-through applications. Evidence of this issue can be seen in the water phantom in the bottom-right image of Figure 4.1. TOPAS demonstrated only a slight increase in fragility, but substantial changes in its chemical properties raise concerns about its long-term performance, especially under higher doses that exceed the range of this study. Materials such as Rexolite and C-552 proved to be completely functional even though subtle changes in some properties were observed.

The following materials showed the most resistance to radiation and are therefore recommended to use for UHDR applications: CPS, PEEK, Graphite and PEEK ELS. CPS is highly recommended for see through applications, as its properties remained unchanged except for slight coloration around dose levels of 1 MGy. It represents a more durable alternative to PMMA, which is currently widely used for such purposes. For non-conductive, non-transparent applications, PEEK proved to be the most durable option, with only minor discoloration observed. For further evidence, the electron experiment holder was made entirely of PEEK, withstanding cumulative doses exceeding 25 MGy without visible damage, as supported by [178]. For conductive applications, graphite remained a durable choice, as no significant changes in chemical, mechanical or conductive properties were observed. While minor surface changes were observed in SEM analysis, these could not be correlated with dose levels or dose rates. Though less conductive, PEEK ELS is also a viable alternative to graphite for conductive applications as all properties remained completely unaffected.

Several additional observations regarding material behavior under UHDR conditions were made in this study due to the variety of conditions tested. Test repeated two years after irradiation revealed recovery effects [41] in the optical and chemical properties of some materials, suggesting that for less exhaustive use, materials irradiated at similar doses as in this study may have extended lifespans in real applications. Chemical analysis of PMMA samples indicated that the type of particle used during irradiation did not influence material degradation; similar dose levels resulted in comparable radiation damage, which is consistent with findings reported in the literature [60].

Regarding dose rate effects, type 'E' samples irradiated with electrons showed no significant difference in damage when comparing the different dose rates explored, suggesting that UHDR does not inherently produce more damage. Instead, UHDR enables higher total doses to be achieved more efficiently. However, under conventional use, healing effects may contribute to enhanced material durability over time.

Experiments with protons consistently showed that the highest damage in the materials occurred in experiment P2, followed by P3, P4, and P1. This order did not correlate with either instantaneous or average dose rates but rather with longer irradiation times. These findings suggest that heat damage contributed to the material degradation, which may explain the observed results. Supporting this explanation, type 'P' samples were irradiated in air, while type 'E' samples were irradiated in water, which dissipated heat more effectively and protected them from heat damage. We want to highlight that even subtle differences can be

observed due to the thermal effects in type 'P' samples, the dominant degradation mechanism observed in this study was dose-dependent rather than dose rate dependent.

Notably, the temperature increase due to radiation varies depending on the heat capacity of different materials, with graphite experiencing approximately 1.4 mK Gy^{-1} [167]. While specific experimental values for the temperature rise due to radiation in PMMA and PEEK are not available, calculations based on their heat capacity suggest similar values: approximately 0.893 mK Gy^{-1} for PMMA (derived from the reported heat capacities of NIST [133, 146]) and 0.917 mK Gy^{-1} for PEEK (derived from [38, 156]). This suggests that the temperature increase due to radiation is comparable for both materials. The difference in damage observed between PMMA and PEEK, despite their similar heat capacities, highlights that the resistance of polymers depends mainly on their chemical structure. The most resistant materials in this study (CPS, PEEK, Graphite and PEEK ELS) have in common aromatic rings in their composition, that enhances their resistance to radiation [59].

In this study, the total dose significantly surpasses the integrated doses that different dosimetry devices typically receive over their lifetime. However, due to the challenges in UHDR dosimetry, extensive studies are required to properly characterize UHDR beams. Furthermore, for clinical translation, certain measurements would possibly require prolonged irradiation times, for instance: relative dosimetry, where PDD curves or field size measurements with ICs are necessary for commissioning, making the accumulation of high doses in QA devices at UHDR unavoidable in practice. Currently, in UHDR beams, such prolonged irradiation times with ionization chambers are not feasible due to detector stress and radiation protection constraints. Consequently, relative dosimetry at UHDR is primarily performed with radiochromic films. However, relying on passive detectors is cumbersome for clinical routine, and radiochromic films themselves exhibit limitations, such as quenching effects in particle beams, that can complicate accurate PDD determination.

4.5 Conclusions

The findings of this study emphasize the complexity of radiation damage mechanisms and the importance of selecting adequate materials for UHDR applications. Evaluating multiple material properties and irradiation conditions is vital as irradiation-induced alterations, often not visible through simple observation, can significantly impact dosimetry accuracy, device calibration, and overall functionality. The still-developing state of UHDR dosimetry and the need of exhaustive beam

characterization for clinical translation of FLASH therapy make UHDR inherently associated with high radiation doses to QA devices in practice.

It has been observed that materials with aromatic rings in their chemical structure exhibit the highest stability under radiation, as demonstrated by the most resistant materials in this study. Depending on the application, different materials are recommended: CPS for transparent applications, PEEK for non-transparent and non-conductive applications, graphite for conductive applications, and PEEK ELS for lower-conductivity applications. As previously noted in Ref. [86], a polymer's resistance under ionizing radiation can be predicted if its macromolecular structure is well understood.

Chapter 5

Developing a dual gap ionization chamber

This chapter details the design, development, and experimental evaluation of the proposed dual-gap ionization chamber (DGIC) prototype. It covers the operating principle, optimization process, and performance testing across different beam types and delivery modes. The content presented in this chapter corresponds to the article: The Dual Gap Ionization Chamber: A novel Ionization Chamber design for reference dosimetry to automatically correct for recombination losses in emerging radiotherapy modalities. Submitted for publication.

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Summary

Objective: Current dosimetry protocols typically recommend multiple measurements to determine recombination correction factors (k_s), increasing the time required for dose measurements in the quality assurance workflow. We propose a novel dual-gap ionization chamber (DGIC) design for reference dosimetry featuring two air gaps of different thicknesses within a single device. This design enables the determination of k_s directly from the same measurements required to determine absorbed dose-to-water. Thus, eliminating the need for separate measurements to correct for recombination losses. The approach relies on analyzing the charge ratio between the two gaps, which can also be correlated with the average dose rate under Ultra High Dose Rates (UHDR) and dose per pulse (DPP) under Ultra High Dose per Pulse (UHDP) conditions.

Approach: A DGIC prototype with electrode distances of 1 and 0.6 mm was developed and tested using different beam qualities: (1) a 240 MeV/u clinical carbon ion beam at conventional dose rates, (2) a 226 MeV continuous proton beam with a current between 5 and 800 nA at the cyclotron exit, where the maximum approximately corresponds to an average dose rate of 200 Gy/s in the treatment room and (3) a 9 MeV electron beam with a DPP from 0.03 to 4.2 Gy, a frequency of 60 Hz and a pulse duration between 0.7 – 3.9 μ s. k_s -factors were derived for the top cavity of 1 mm gap using the DGIC method and compared against the following: For proton and carbon ions, comparisons were made with the Jaffé plot method. For the electron beam, it was compared with a dose rate independent device, a flashDiamond detector, and the integrated current transformer of the LINAC.

Main Results: A DGIC prototype was able to successfully correct for recombination losses under different beam modalities: for initial recombination in a clinical carbon ion beam, volume recombination in UHDR proton beam with average dose rates of 200 Gy/s and in UHDP electron beams up to a DPP of 4.2 Gy.

Significance: A DGIC design and its inherent method provides a practical and accurate way of determining dose and dose rate in emerging radiotherapy treatment modalities.

5.1 Introduction

Air-filled Ionization Chambers (IC) are the gold standard for reference dosimetry in radiotherapy (RT) and are widely endorsed by international dosimetry protocols such as IAEA TRS-398 [78] and AAPM TG-51 [10]. Their operation is based on measuring the charge generated by ionizing radiation within the air cavity, which is then corrected by various influencing factors and converted to absorbed dose to water using a calibration coefficient. One of these corrections is the ion recombination factor (k_s), which accounts for charge losses due to ion recombination prior to collection.

Ion recombination is typically categorized into initial recombination, occurring between charge carriers from a single ionizing particle track, and volume recombination, occurring between carriers from different tracks. Initial recombination depends on the Linear Energy Transfer (LET) of the incident radiation particle and is described by Jaffé's theory [88, 89], while volume recombination is dose rate dependent and modeled by Boag's theories for both pulsed [19, 22, 21] and continuous beams [23].

Due to chamber to chamber variability and the sensitivity of theoretical models to physical parameters, generic or simulated k_s values cannot be confidently used. Instead, experimental determination for each specific IC under use is prescribed [78]. Among the different experimental methods to determine it, the two-voltage method (2VM), traditionally endorsed in TRS-398 for photon and electron beams, is the most widely used. However, its applicability becomes limited in emerging (high LET beams and UHDR/UHDP) beam modalities.

In high-LET particle beams, typically used for their higher radiobiological effect, initial recombination may be significant. Under these conditions, the 2VM is limited, as it should be used only if the inverse of the charge collected ($1/M$) is linear with the inverse of the applied voltage ($1/V$), a condition often unmet [78]. Alternatives such as the three-voltage linear method (3VM) [161] or the Jaffé plot method (now included in the revised version of the TRS-398), provide better accuracy but demand multiple measurements and corrections for charge multiplication for ICs with smaller air gaps [164].

Ultra High Dose Rates (UHDR) or Ultra High Dose Per Pulse (UHDP) are beam delivery regimes required for FLASH radiotherapy. Due to the FLASH effect, consisting in the observation of a sparing effect on healthy tissue coupled to efficacious antitumor effect [30, 188, 187], FLASH-RT is of increasing interest in the radiotherapy field. In FLASH-RT, dose rates exceed conventional levels by sev-

eral orders of magnitude ($\gtrsim 40$ Gy/s) [194]. Under such conditions, recombination losses are substantial and compromise the validity of the 2VM.

For UHDR proton beams, isochronous cyclotrons delivering quasi-continuous radiation have been more extensively investigated. In this case, volume recombination dominates and can be corrected if a linear behavior between $1/M$ and the inverse squared of the voltage ($1/V^2$) is observed [177]. However, in the extreme case of UHDP electron beams, recombination losses become even more pronounced, and all previous endorsed methods fail to determine k_s .

Given these challenges, there has been significant interest in exploring other detector types. Despite advances, many alternatives such as alanine [28], gafchromic films [113, 186], optically stimulated luminescence films [127, 181], and inorganic or organic plastic films [183, 182] face limitations in real time readout and some of them show limited dose rate dependency [96]. More promising developments include silicon carbide detectors [61, 134, 114], calorimeters [26, 115] and diamond-based detectors [104].

Nevertheless, a lot of investigations are done to try to use ICs in UHDR and UHDP conditions. Recent research efforts on this class of detectors entail simulation based studies [39, 103, 147], semi-analytical approaches [14], extensions of theoretical models [58], and experimental investigations of multiple ICs under UHDP conditions [29]. Additional approaches focus on IC design improvements, such as using gases with low recombination rates [51], extremely reducing the air gap thickness [66, 112], or developing semi-empirical methods for correcting recombination in standard ICs [150]. Overall, the main limitations of using conventional ICs under emerging modalities, particularly in UHDR conditions, are the complexity and labor intensive nature of experimentally determining k_s for each specific chamber, as well as unresolved issues that persist in the highest dose per pulse (DPP) regions of the UHDP regime.

In this work, we propose a novel IC design for reference dosimetry, the Dual Gap Ionization Chamber (DGIC), along with its inherent method [153], already implemented in [169] with the dose monitoring ICs in the nozzle of a proton therapy system. This design integrates two ionization chambers within a single device, allowing for simultaneous reading of collected charges. By analyzing the variation in the charge ratio between the two gaps, the recombination correction factor k_s can be derived directly from the same measurements used to determine absorbed dose to water, thereby eliminating the need for separate measurements to account for recombination losses.

Since the method does not require any specific linear relationship between the inverse of the collected charge and inverse of the applied voltage, it is particularly suited for non-conventional conditions, including high-LET beams, UHDR and specific UHDP domains. Furthermore, because the DGIC uses the response from both cavities, it can potentially provide additional information, such as real time dose rate estimation through charge ratio variation, thus functioning as both for dose and dose rate determination.

5.2 Materials and methods

5.2.1 Prototype design

The Dual Gap Ionization Chamber (DGIC) consists of two ICs with a different air gap size in face-to-face position separated by a thin layer of material within a single device. The DGIC prototype was designed according to the recommendations provided by TRS-398, which include: the use of near water equivalent materials, a vented chamber design, a collecting electrode diameter not exceeding 20 mm, a cavity height not greater than 2 mm, and a guard ring width not smaller than 1.5 times the cavity height. Following those guidelines, a DGIC prototype was constructed (see Figure 5.1). To avoid damage and considering its potential use in UHDR conditions, the prototype was entirely made of Polyether ether ketone (PEEK) and graphite [136]. The air gap thickness was set at 1 mm for the top cavity and 0.6 mm for the bottom cavity; further discussion on the selection of these air gaps is provided in Section 5.4.1.



Figure 5.1: External appearance of a DGIC prototype. The dimensions are comparable to those of a standard ionization chamber, though the chamber outer diameter is slightly larger (64 mm) to facilitate prototype assembly.

To limit potential dose gradients between both gaps, the piece of the ground electrode in the top chamber also serves as part of the entrance window of the bottom chamber, as illustrated in Figure 5.2.

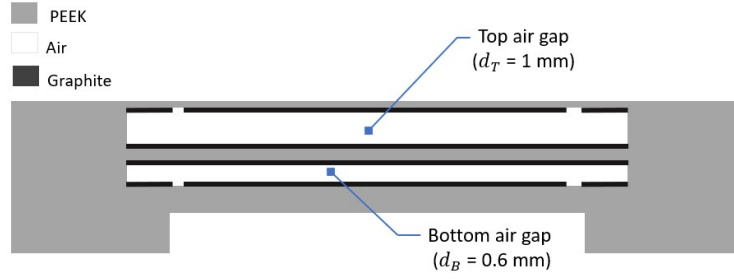


Figure 5.2: Schematic representation of the DGIC prototype geometry. The top air cavity has an electrode spacing of 1 mm (d_T), while the bottom cavity has a spacing of 0.6 mm (d_B). The two cavities are positioned face-to-face.

5.2.2 Principle of use

The method used to determine the ion recombination correction factor is based on the semiempirical relation [153]:

$$\frac{1}{k_s^T} = 1 - \frac{1 - \left(\frac{M_T}{M_B}\right)_N}{G} \quad (5.1)$$

In this formulation, k_s^T is the ion recombination correction factor for the top gap, M_T and M_B are the charge reading in the top (T) and bottom (B) cavities, respectively. The ratio M_T/M_B is normalized by the ratio of their respective amplification factors, indicated by the subscript N , to account for differences in the signal between the two gaps. This normalization, adapted for reference dosimetry, is related to the ratio of their respective calibration coefficients (N_{D,w,Q_0}), which depends on the active volumes of the chambers and must include beam quality correction factors (k_{Q,Q_0}). The subscripts Q and Q_0 denote the user beam quality and the reference beam quality respectively. The normalized ratio is given by:

$$\left(\frac{M_T}{M_B}\right)_N = \frac{\frac{M_T}{M_B}}{N} = \frac{\frac{M_T}{M_B}}{\frac{N_{D,w,Q_0}^T k_{Q,Q_0}^T}{N_{D,w,Q_0}^B k_{Q,Q_0}^B}} \quad (5.2)$$

If the active volumes of both gaps have the same radius and no recombination losses are present, the signal amplification is ideally governed by the gap spacing ratio between the top (d_T) and bottom (d_B) cavities (d_T/d_B), as noted by [169].

However, due to manufacturing tolerances and assembly variability, the actual gap ratio may differ from the theoretical value. Although the calibration coefficients should ideally compensate for these differences, uncertainties in N_{D,w,Q_0} determination and the presence of charge multiplication in small gaps complicate this way of calibration. To improve accuracy, it is more reliable to determine the amplification coefficient N as the charge ratio corrected by charge multiplication, as described in [164], and subsequently applying a reliable method for correcting recombination losses in the calibration beam. Following TRS-398 recommendations, the use of the 2VM or Jaffé plot method in a ^{60}Co beam provides accurate results.

The parameter G in Equation 5.1 is a proportional factor obtained from a first-order Taylor expansion of the specific recombination theories. It depends on the type of recombination, the gap spacing and applied voltage (this last quantity is denoted as V_T for the top cavity and V_B for the bottom cavity). When only initial recombination is present, or when the beam is considered pulsed (occurring when the pulse duration is shorter than the collection time of the IC and this collection time is shorter than the time between pulses [142]), the expression for G is:

$$G_{puls/initial} = 1 - \frac{d_B^2/V_B}{d_T^2/V_T} \quad (5.3)$$

If the above conditions are not satisfied, the beam is considered as continuous or quasi-continuous [142], and the corresponding expression for G is:

$$G_{cont} = 1 - \frac{d_B^4/V_B^2}{d_T^4/V_T^2} \quad (5.4)$$

Further information on the derivation of these expressions is provided in the supplementary materials.

Note that N is a parameter that modulates the independent term of the calibration, whereas G modulates the slope. Once N and G are determined, Equation 5.1 allows the determination of k_s^T from a single simultaneous measurement of the charge collected in both gaps, which can be practically achieved simultaneously using two electrometers or a dual channel electrometer.

Another application of the DGIC, taking advantage of its ability to simultaneously measure the charge collected in both gaps, is its potential use as a dose rate meter. In pulsed beams, it can be used to determine the instantaneous dose rate or the dose per pulse, while in continuous beams, it allows the measurement of the average dose rate. The underlying principle is similar to that used for the determination of k_s^T : the ratio of charges measured in the two gaps must be first

normalized, as previously described, and then related to the dose rate using a calibration derived conversion factor. The dose rate measured by the DGIC is then given by:

$$DR_{DGIC} = \frac{\left(\frac{M_T}{M_B}\right)_{norm} - 1}{CF} \quad (5.5)$$

Where CF is a conversion factor that converts the normalized charge ratio to dose rate (DR) and $norm$ is defined as in Equation 5.2. To determine CF for a given beam, the same expression is used but with the dose rate obtained from an independent method. Once calibrated, the DGIC offers a practical, real time method to determine the dose rate in UHDP and UHDR conditions.

5.2.3 Modeling of the DGIC

Different calculations were performed to model the behavior of the DGIC under various conditions. These included understanding the operating principles of the method, optimizing air gap and voltage configurations, and determining relevant parameters such as the beam quality correction factors k_{Q,Q_0} .

A Monte Carlo based simulation tool was used to determine k_s in scenarios where analytical solutions to theoretical models are not found, which is the case for very low or very high k_s -values. Further details on the implementation, intercomparison, and validation of this simulation tool can be found in [137] or Chapter 3.

To calculate the ratio of the beam quality correction factors as required for Equation 5.2, the beam quality correction factors k_{Q,Q_0}^i for each of the gaps (T: Top and B: Bottom) were calculated following the formalism described in [11]:

$$k_{Q,Q_0}^i = \frac{(D_w/\bar{D}_{air})_Q \bar{w}_{air,Q}}{(D_w/\bar{D}_{air})_{Q_0} \bar{w}_{air,Q_0}} \quad (5.6)$$

where D_w denotes the local absorbed dose in water, $\bar{D}_{air}$ the averaged absorbed dose in the sensitive air volume of the IC and $\bar{w}_{air}$ the mean energy to create and ion pair in air. Following Equation 5.6, if the effective depth of measurement is the same for both cavities, then the ratio of the k_{Q,Q_0} factors between the top and bottom cavities is given by:

$$k_{Q,Q_0}^R \stackrel{\text{def}}{=} \frac{k_{Q,Q_0}^T}{k_{Q,Q_0}^B} = \frac{(D_w/\bar{D}_{air})_Q}{(D_w/\bar{D}_{air})_{Q_0}} \quad (5.7)$$

The Monte Carlo simulation toolkit Geant4-v11.2 [9] was used to derive $\bar{D}_{air}$ values within the DGIC which was modeled using the material properties summarized in Table 5.1.

Material	I (eV)	ρ (g cm ⁻³)
Air	85.7	0.0012
Graphite	81.0	0.93
PEEK	74.1	1.31
Water	78.0	0.9982

Table 5.1: Material properties used for the simulation. Each material has its corresponding ionization potential (I) and density (ρ).

All the methodology on the Monte Carlo calculation of k_{Q,Q_0} factors is based on [77] including the different parameters presented in Table 5.2 as well as the physics list used for gamma and proton simulations. The physics list for protons was used for electrons, and also for carbon ions simulations for which the two following constructors were included: *G4RadioactiveDecayPhysics* and *G4IonElasticPhysics*, following [98]. For electrons, the beam parameters were based on the experimental conditions described below.

For each air cavity composing the DGIC, the corresponding reference point of measurement was defined at the inner center of the upper surface of the cavity. For the different particles, the positioning of the chamber was always accounting for the Water Equivalent Thickness (WET) of any non-water volume placed between the source and the cavity considered. Therefore, for top cavity simulations, the WET of the entrance window was considered, while for the bottom cavity simulations, the WET of the entrance window and the foil separating the two cavities were both considered.

Parameter	Gamma	Electron	Proton	Carbon
Beam shape	Square	Circle	Square	Square
Beam direction	Divergent	Parallel	Parallel	Parallel
Beam dimensions	10x10 cm ²	$r = 4.5$ cm	10x10 cm ²	10x10 cm ²
Beam energy	[126]	6, 9, 10, 12 MeV	226 MeV	240 MeV/u
Phantom size	20x20x20 cm ³	20x20x10 cm ³	20x20x10 cm ³	20x20x10 cm ³
Measurement depth	5 cm	1.5 g cm ⁻²	2 g cm ⁻²	1 g cm ⁻²
Cut Phantom	500 μ m	500 μ m	500 μ m	500 μ m
Cut Volume	1 μ m	1 μ m	1 μ m	1 μ m
dR/R - finalRange	0.003 - 1 nm	-	0.05 - 100 nm	-
Step limit	-	-	1 mm	-

Table 5.2: Summary of the simulation setups used for the Monte Carlo calculation of the k_Q factors. The symbol “-” characterizes the use of the default value for the parameter considered.

5.3 Experimental conditions

Experimental campaigns were performed at different centers to investigate the behavior of the DGIC in multiple conditions and beam qualities: (1) A ^{60}Co source at the IBA Dosimetry Secondary Standard Laboratory (SSDL) in Schwarzenbruck, Germany; (2) a 240 MeV/u clinical carbon ion beam at the MedAustron Particle Therapy Center in Wiener Neustadt, Austria [175]; (3) a 226 MeV quasi-continuous UHDR proton beam at the Fred Hutch Cancer Center in Seattle, USA; and (4) a 9 MeV UHDP electron beam at the University of Antwerp, Belgium. For all experiments, both cavities of the DGIC were connected to two different Dose1 electrometers (IBA Dosimetry). Additionally, for the UHDPP experiment, two different DoseX electrometers (IBA Dosimetry) were used to investigate possible charge saturation caused by the Dose1 electrometers.

Beam	Center	Modality	Energy	Field	Ref. dosimeter
^{60}Co	IBA SSDL	^{60}Co source	~ 1.25 MeV	10×10 cm ²	PPC40
Carbon	MedAustron	Synchrotron	240 MeV/u	6×6 cm ²	PTW-34001
UHDR proton	Seattle	Isochronous cyclotron	226 MeV	8×8 cm ²	PPC05
UHDP electron	Antwerp	LINAC	9 MeV	$\varnothing = 10$ cm	flashDiamond

Table 5.3: Summary of the beams used to investigate the DGIC.

At the IBA Dosimetry SSDL, the DGIC prototype was calibrated with a ^{60}Co source following TRS-398 procedures, with calibrations traceable to the Primary Standards Dosimetry Laboratory (PSDL) of PTB (Germany). The bias voltage over both gaps was set to -300 V during calibration. The top gap was calibrated at its reference depth; for the bottom cavity, the reference depth included the WET of the upper cavity and the thin separation layer between gaps. The ^{60}Co beam was also used to determine the charge multiplication correction factor (called k_{CM}) for each gap, since the small air gaps operated at high voltage makes this correction non-negligible. Following the method described by [164], Jaffé plots ($1/M$ vs. $1/V$) were obtained and fitted with a nonlinear least squares method on the exponential model:

$$k_s k_{CM} = \left(1 + \frac{A}{V} I_{sat} \right) e^{-\gamma V} \quad (5.8)$$

where the first term (parameter A) corresponds to the initial recombination contribution (volume recombination was assumed to be negligible). The value of I_{sat} was estimated using a linear extrapolation of a linear fit from the Jaffé plot with data from $|1/V| = 0.01 - 0.05$ V⁻¹. The second term, exponential with the voltage V , corresponds to the contribution of charge multiplication, where the parameter γ is a chamber-specific factor independent of the beam quality [164].

At MedAustron, the DGIC was tested in a synchrotron-accelerated carbon ion beam to study initial recombination effects. A non-modulated Pencil Beam Scanning (PBS) field of 240 MeV/u (distal range $R_{80} = 35$ cm) was delivered in a 6×6 cm² field with 0.2 cm spot spacing. The DGIC prototype was positioned in a MP1 Manual MR Water Phantom (PTW-Dosimetry, Freiburg, (Germany)) at 1 cm depth in the plateau region, with a ROOS chamber – PTW 34001 (PTW-Dosimetry, Freiburg, (Germany)) placed behind the prototype under investigation to monitor beam fluctuations. To investigate potential contributions from volume recombination, a dose rate variation was introduced through three delivery settings: a 1 s spill duration, a 10 s spill duration, and a 10 s spill duration with a beam intensity reduced by 90%. These configurations corresponded to approximate average dose rates over the entire field delivery at the effective point of measurement of the IC of 25, 2.5 and 0.4 Gy/min, respectively. Jaffé plots were obtained, corrected for k_{CM} previously obtained in ⁶⁰Co, and fitted to the full Jaffé theory for initial recombination, following recommendations from [162], as traditional linear fits can lead to underestimations of experimental k_s -values. The free parameters N_0 and b from Jaffé's model (see Equation 2.21) were optimized and the resulting k_s^T -values were then compared with those obtained using the DGIC method.

At the Fred Hutch Cancer Center, the DGIC was studied under a quasi-continuous 226 MeV proton beam delivered by a cyclotron using an IBA Proteus Plus system. The beam was delivered in an 8×8 cm² scanned field composed of 100 spots of 7.5 mm (1σ). A wide range of beam currents at the cyclotron exit was used (8, 500 and 800 nA), with the highest setting corresponding to average dose rates at the measurement depth of approximately 200 Gy/s. Delivery times were extracted from the system log files, and the total dose was measured independently using an IBA PPC05 (IBA Dosimetry, Schwarzenbruck (Germany)) ionization chamber. Jaffé plots were obtained and corrected for k_{CM} . The resulting k_s^T -values obtained from the DGIC method were compared with those obtained using the Jaffé plot method.

At the University of Antwerp, the DGIC was tested in an UHDP 9 MeV electron beam produced by an ElectronFLASH (EF) LINAC developed by SIT-Sordina (Italy). The beam was collimated with a 10 cm diameter applicator, with effective pulse durations ranging from 0.7-3.9 μ s at a pulse frequency of 60 Hz. The number of pulses was fixed to 4, and the dose per pulse varied from 0.03 to 4.2 Gy. The source to surface distance (SSD) was set to 106 cm. The DGIC was positioned at 14 mm depth. A flashDiamond (fD) detector (PTW-Dosimetry, Freiburg, Germany) was placed immediately after the DGIC, at 1.9 cm. Dose was normalized at the lowest DPP. The Integrated Current Transformer (ICT) of

the EF-LINAC was used to determine the number of pulses delivered. k_s^T was determined by fitting the experimental curves to Petterson's [150] modified [29] semiempirical equation.

5.4 Results

5.4.1 Simulations, calibration and calculations

Figure 5.3 (a) shows the variation of the parameter G from Equation 5.1, for different recombination regimes (initial, volume pulsed and continuous) as a function of the air gap ratio d_B/d_T , for various voltage ratio configurations V_T/V_B between the top (T) and bottom (B) cavities.

A higher G -factor is preferable, as it enhances the charge difference between the two ionization chambers, thereby increasing the sensitivity and improving the accuracy of the method. As shown, G increases when the gap ratio d_B/d_T decreases or when the voltage ratio V_T/V_B is increased. However, reaching G -factor values close to 1 can be practically challenging: Small d_B/d_T ratios require large disparity in the absolute gap sizes, necessitating either very large or very small gaps. Large gaps are unsuitable for UHDR applications, as they lead to excessive recombination effects, and given that, it would surpass the TRS-398 recommendation of 2 mm. Conversely, very small gaps are challenging to manufacture, can compromise the fabrication reliability and lead to larger multiplication effects. Similarly, while increasing V_T/V_B enhances G , similar issues occur: low bias voltages in one gap can result in significant recombination, while excessive high voltages may induce significant charge multiplication effects, which deviate from ideal ionization chamber behavior.

A balanced and practical configuration, which does not deviate much from already existing traditional ICs designs, is achieved by setting the top and bottom gaps to 1 and 0.6 mm, respectively, with an equal bias voltage of -300 V. This corresponds to a theoretical gap ratio $d_B/d_T = 0.6$ and a voltage ratio $V_T/V_B = 1$, which results in theoretical gains of $G_{cont} = 0.87$ and $G_{puls/ini} = 0.64$.

Figure 5.3 (b) shows the theoretical variation of the charge collection efficiencies (f , inverse of k_s) for a continuous proton beam with the chosen configuration for the DGIC prototype ($d_T = 1$ mm, $d_B = 0.6$ mm, $V_T = -300$ V and $V_B = -300$ V) as well as the components of Equation 5.1 versus the dose rate. The G factor remains constant across a large dose rate range, showing the feasibility of using this method even at UHDR.

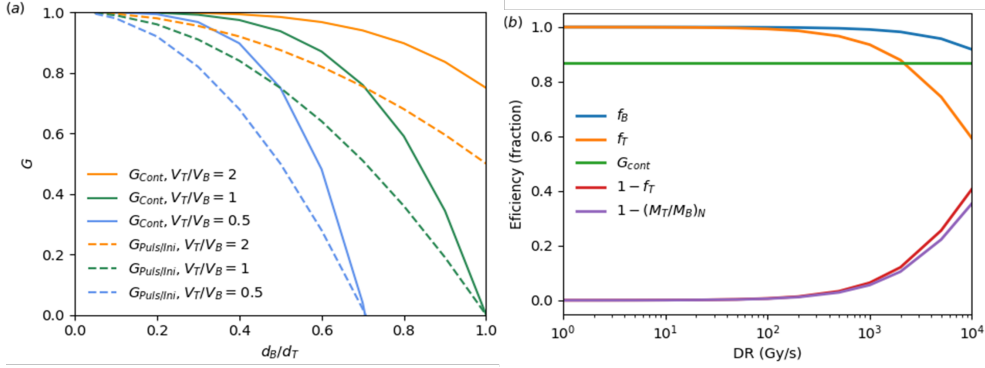


Figure 5.3: (a) Theoretical dependence of the G -values on the theoretical gap ratio d_B/d_T for volume recombination in quasi-continuous beam (continuous lines) and pulsed beams or initial recombination (dashed lines) for different voltage ratios between the top and bottom cavities V_T/V_B . (b) Theoretical variation of the efficiency in a continuous proton beam of the top gap (orange line), the efficiency of the bottom gap (blue line), the nominator (purple line) of Equation 5.1, denominator (red line) of Equation 5.1, and G_{cont} (green line) of Equation 5.1 as a function of the dose rate (DR) for the specifications of the DGIC prototype developed in the present study.

The DGIC was successfully calibrated in a ^{60}Co beam. The relative type-A uncertainty, estimated from the standard deviation of the mean of the measured current was lower than 0.1%. The gamma parameter of Equation 5.8 (i.e. charge multiplication effect coefficient) obtained for the top and bottom cavity were $\gamma_T = (2.13 \pm 0.16) \cdot 10^{-5} \text{ V}^{-1}$ and $\gamma_B = (3.54 \pm 0.21) \cdot 10^{-5} \text{ V}^{-1}$, respectively. As expected, the smaller gap, (i.e. bottom cavity) yielded higher charge multiplication, and the larger gap (i.e. top cavity), smaller. At the calibration voltage of -300 V this resulted in a charge multiplication correction of about 0.6% for the top cavity and a 1.1% for the bottom cavity. This k_{CM} correction factors are applied throughout the entire study, assuming beam quality independency, in cases where the DGIC is used in a different bias voltage as the one it was calibrated.

At the bias voltage of -300 V, the measured charge ratio $M_T/M_B = 1.562$ was corrected by $\frac{k_s^T}{k_s^B} \cdot \frac{k_{CM}^T}{k_{CM}^B} = 1.004$ which results in an experimental normalization value of $N = 1.568 \propto d_T/d_B$. Accordingly, the experimentally determined G -factors were $G_{cont}^{exp} = 0.835$ and $G_{puls/ini}^{exp} = 0.593$.

As the DGIC was tested in different beam qualities: electron, proton and carbon ion beams, Monte Carlo simulations were carried out to determine the beam quality correction factor of each of the gaps, to determine the ratio as needed for Equation 5.2. The values of k_{Q,Q_0}^R for the different beam qualities are presented in Table 5.4. All values, regardless of the particle beam type, agree with each other and with unity within the 1σ level. Consequently, in the following analysis, $k_{Q,Q_0}^R=1$ is adopted as a reasonable assumption.

Particle	Energy (MeV)	k_{Q,Q_0}^R
Electron	6	1.000(6)
	9	1.002(6)
	10	1.003(6)
	12	1.000(6)
Proton	226	1.004(6)
Carbon	240/n	1.001(6)

Table 5.4: Numerical k_{Q,Q_0}^R values for electrons, protons and carbon ions in this study. The values with parenthesis correspond to one standard deviation of the last digit.

5.4.2 Correction for initial recombination

Figure 5.4 (a) shows the Jaffé plots measured for the top cavity of the DGIC prototype in a 240 MeV/u carbon ion beam at the three different dose rates investigated. The relative type-A uncertainty of the measured current was 0.1% or smaller for the bias voltage of -300 V and increases for lower voltages which explain the differences observed between the Jaffé plots for different dose rates. Monte Carlo simulations for k_s determination were conducted for the three different dose rates. As shown in Table 5.5, there is a minimal contribution of volume recombination, between 0.4 – 1.8% of the total recombination. This confirms that the differences observed are due to experimental variability, and that only initial recombination is present.

Figure 5.4 (b) shows the variation of k_s^T with $|1/V|$ for the different methods: Jaffé's model, Jaffé plot method and DGIC method. Fit to the Jaffé's theoretical model parameters, the values found were: $N_0 = 91899 \pm 4225$ ion pairs/cm and $b = 0.0045 \pm 0.0014$ cm from Equation 2.21, in line with expected values [162]. To obtain k_s^T through the DGIC method, N -value and G_{ini} -experimental values for the initial recombination were applied, obtained from previous calibration in ^{60}Co . No k_{Q,Q_0}^R correction was applied as previously explained. There is good agreement between the different methods, with maximum relative differences of 0.5%.

Voltage (V)	0.4 Gy/min			25 Gy/min		
	Total k_s	% Initial	% Volume	Total k_s	% Initial	% Volume
300	1.006(1)	99.6	0.4	1.006(1)	99.6	0.4
100	1.017(2)	99.5	0.5	1.017(2)	99.5	0.5
50	1.031(3)	99.5	0.5	1.031(3)	99.5	0.5
20	1.068(4)	99.4	0.6	1.069(3)	98.2	1.8

Table 5.5: Theoretical calculations with the Monte Carlo simulation for k_s determination of the contribution of initial and general recombination in the top gap of 1 mm for the smallest and largest dose rates investigated in the 240 MeV/u carbon ion beam, for different voltages. The calculations show a negligible contribution of the volume recombination.

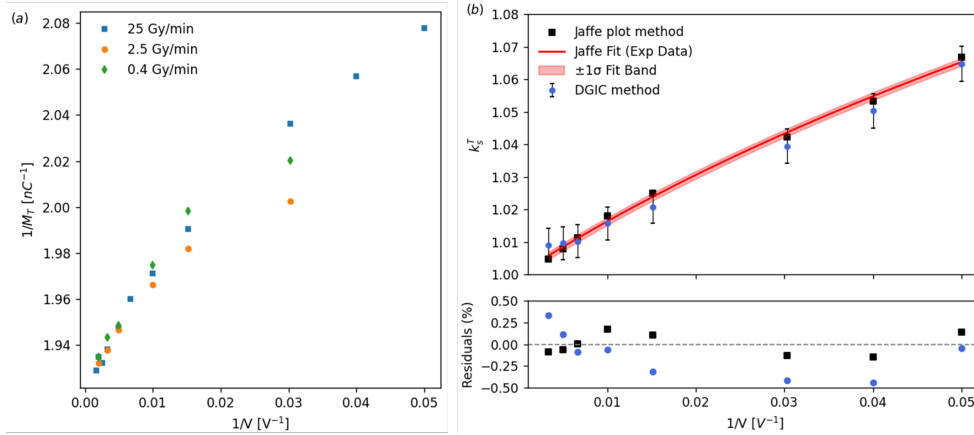


Figure 5.4: (a) Jaffé plots from the top cavity for the various dose rates investigated across different experimental campaigns. (b) Variation with $|1/V|$ of Jaffé plot method (black points), k_s^T -values obtained by fitting to Jaffé theory (red line) including the 1σ confidence band, and k_s^T -values determined with the DGIC method (blue dots).

5.4.3 Correction for volume recombination

Protons UHDR, continuous beam

To determine k_s^T using the DGIC method in a 226 MeV proton beam, experimental values for the N -value and G -value (specifically G_{cont} , as volume recombination in a quasi-continuous beam is studied) were applied. As in the previous section, k_{Q,Q_0}^R -value was taken as 1. The relative type-A uncertainty of the mea-

sured current was around 0.1% for the lower voltage ranges (-500 to -100 V). For smaller voltage ranges, the standard deviation of the averaged measured current was between 0.2 and 0.4%.

Figure 5.5 (a) shows the variation of k_s^T with $|1/V|$, calculated using both the DGIC method and the Jaffé plot method. As expected in a quasi-continuous beam where volume recombination dominates, a quadratic trend of k_s versus $|1/V|$ is observed. At the lowest dose rate (i.e. 5 nA), in conventional mode, small recombination losses (below 1% at the bias voltage of -300 V) are present. As the dose rate increases, k_s^T also increases up to 1.6% (at the bias voltage of -300 V), indicating the expected dose rate dependence of k_s .

The agreement between the two methods at -300 V (residuals at $|1/V| = 0.0033 \text{ V}^{-1}$ in Figure 5.5 (a)) is within 0.5% across all three dose rates. For smaller bias voltages (larger $1/V$ values in Figure 5.5 (a)), the agreement between the methods differs, which may be attributed to the larger uncertainties associated at lower voltages as discussed in Appendix 5.A.3.

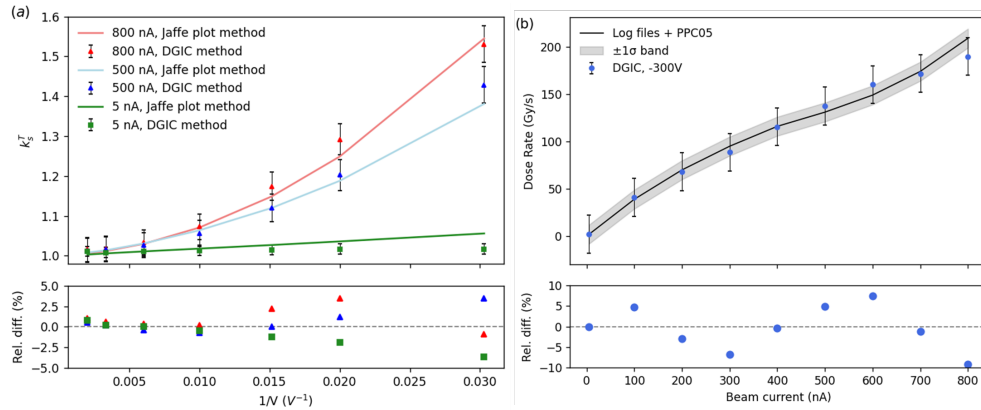


Figure 5.5: (a) Variation of k_s^T with $|1/V|$ for the three currents investigated: 800 nA (corresponding to about 200 Gy/s, shown in red), 500 nA (corresponding to an average dose rate of about 130 Gy/s, shown in blue) and 5 nA (corresponding to an average dose rate of about 15 Gy/min, shown in green). Values were obtained using the Jaffé plot method (solid lines) and the DGIC method (scattered points). (b) Dose rate determined using the DGIC method (blue points) compared to the reference method based on PPC05 measurements and log files analysis (solid line). The lower part of both figures represents the relative differences between the DGIC method and the reference.

Figure 5.5 (b) presents the average dose rate obtained via the DGIC method, according to Equation 5.5. The overall agreement with the reference is around 5%. The reference dose rate was determined by measuring the integrated dose at the lowest dose rate with a PPC05 and the delivery time of each spot through log-file analysis. The main sources of uncertainty arise from the type-A propagation of error the type-A uncertainty in dose determination with the PPC05, the determination of the delivery time, and differences in IC placement, contributing to an estimated combined uncertainty of approximately 10%.

The conversion factor for the DGIC method in Equation 5.5 was obtained at a beam current of 5 nA. As shown in Figure 5.5 (b), the comparison between both methods, which agree within 5%, fall within the estimated uncertainty range, particularly given the large uncertainty in the method used for dose rate determination.

Electrons UHDP, pulsed beam

k_s^T was determined with the DGIC method following the procedure in previous experimental results sections, but using G_{puls} as this part addresses the case of volume recombination in a pulsed beam. The fD DPP values are shifted to lower values relative to those obtained with the DGIC, since the fD was positioned after the DGIC prototype, in the region of the PDD curve where the dose decreases with depth. To enable comparison of DPP values beyond the range measured with the fD, its response curve was extrapolated, given that its response is linear with dose. The relative type-A uncertainty in the measured current was around 1% for the fD and approximately 0.6% for the DGIC prototype.

Figure 5.6 (a) shows the dose determined in the 9 MeV UHDPP electron beam with the DGIC as a function of the DPP obtained with two DoseX electrometers, comparing results obtained without correction for recombination losses, with those corrected using k_s^T , and with the dose measured with the flashDiamond (fD). Not correcting for recombination can lead to a significant underestimation of dose (up to 90% at DPP values around 4.2 Gy). Applying the DGIC method to correct for recombination enables improved dose determination. Figure 5.6 (b) shows the same plot if two Dose1 electrometers are used, where the response of the DGIC saturates around 1.2 Gy as the instantaneous current produced by the radiation pulse exceeds the maximum current supported by the electrometer [66].

Figure 5.7 shows k_s^T obtained with the DGIC method and compared with the Petersson semiempirical model, with fitting parameters found to be $\alpha=0.83$ and $\beta=0.35$, consistent with values reported in the literature [29, 150].

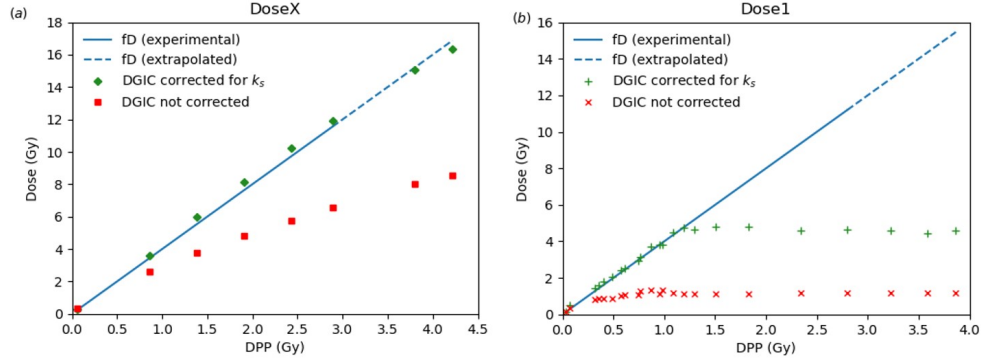


Figure 5.6: (a) Dose versus DPP obtained experimentally with the flashDiamond (fD, solid blue line), extrapolated values (fD, dashed blue line), DGIC corrected for recombination losses (green diamonds) with the DGIC method, and DGIC not corrected for k_s (red squares) obtained with two DoseX electrometers. (b) Similar graph but obtained with two Dose1 electrometers where in this case the green crosses represent the DGIC corrected for recombination losses with the DGIC method and the red plus symbol represent the uncorrected values.

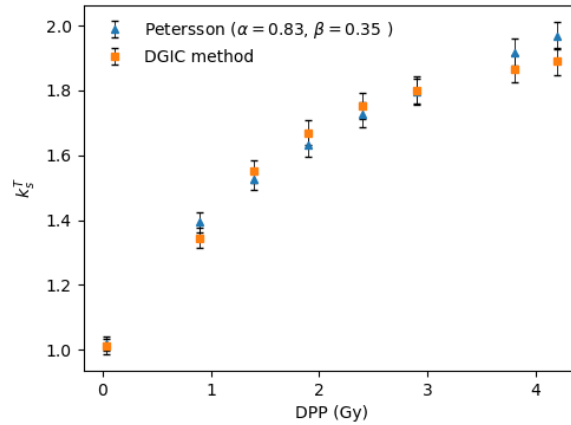


Figure 5.7: k_s^T -values determined with the Petersson semiempirical model (blue triangles) compared with the DGIC method (orange squares) and its corresponding uncertainties in k_s determination.

5.5 Discussion

The DGIC method presents a novel and practical approach to correct for ion recombination in ionization chamber thanks to its unique double air gap design within the same device. By measuring the ratio of collected charges in each gap at their respective bias voltage, the method enables the determination of the recombination correction factor k_s for one of the gaps in a single measurement, in contrast with other commonly used methods. While the 2VM remains the standard recommended in TRS-398, the updated guidelines acknowledge the need for more accurate alternatives in particle beams. Methods such as the Jaffé plot method, while more accurate, require multiple measurements with varying voltages, associated with longer stabilization times of the IC, making them less practical for routine clinical use.

The DGIC can be easily calibrated in a ^{60}Co beam. However, improved accuracy can be achieved by directly evaluating the charge ratio, ideally without recombination losses, while accounting for charge multiplication and any minimal recombination present. This approach makes the DGIC method adaptable to a wide range of conditions, capable of correcting both initial and volume recombination, covering UHDR conditions and, to a limited extent, UHDP.

In continuous UHDR proton beams, with average dose rates up to 200 Gy/s, the DGIC method demonstrated accurate recombination correction and enabled dose rate estimation, if prior calibration is performed. While these dose rate estimates are valuable, the uncertainties observed in this study indicate that more precise methods would be needed for applications requiring high accuracy in dose rate determination. Addressing this uncertainty is beyond the scope of this study but remains an area for future improvement.

For UHDPP electron beams the DGIC method has shown to work for the full range of DPP covered in this study. Initially, measurements beyond 1.2 Gy per pulse with Dose1 electrometers appeared unreliable, suggesting a possible breakdown due to either saturation of the electrometers or space-charge screening effects that distort the effective electric field and violate the assumption of a constant G-value. The latter explanation, however, would be expected to produce a more gradual failure of the method. Repeating the experiment with DoseX electrometers confirmed that the method itself remains valid, and that the apparent deviation was caused by limitations of the electrometer. This highlights the critical importance of using equipment compatible with UHDPP conditions, as inadequate instrumentation can lead to erroneous characterization of detector response and misleading conclusions about the underlying physical behavior.

In the case that the method could break down due to space charge screening effects, which distort the effective electric field and violate the requirement of a constant G-value, it would be possible to model G as a function of dose rate and establish a calibration curve. This approach would require DPP external information, allowing to determine k_s^T -values beyond this range, however the magnitude of the correction and associated uncertainty becomes unreasonably large, limiting practical application. However, this approach raises broader questions regarding the reliability and acceptable thresholds for k_s under extreme dose rate scenarios.

Reducing the air gap could extend the operational range by minimizing space charge effects, as explored in other studies [66, 112]. However, such extreme designs would likely increase charge multiplication [164] and present challenges in manufacturing a DGIC with high precision.

The theoretical basis of the DGIC method also suggests potential for estimating LET, in a manner analogous to the dose rate estimation. This has been explored in liquid ionization chambers [71, 179], but could not be achieved with the present geometrical configuration due to the small air gaps used in the current design, optimized to minimize recombination in UHDR conditions. Previous work by [162] demonstrated that LET effects on k_s become detectable with larger air gaps (e.g., 2 mm air gap operated at low voltages), though such configurations introduce significant recombination, and render the system incompatible for use at UHDR.

While the current design lacks sufficient sensitivity to k_s variations due to LET with depth, the underlying concept could be adapted to other contexts, such as large-area ionization chambers used in hadron therapy [105, 138]. In such applications, the same dual-gap principle could be used to simultaneously assess dose and LET through depth dose curve measurements. This possibility, though not addressed experimentally in this study, offers an interesting direction for future work.

Appendix 5.A.3 details the main sources of uncertainty considered in this work. For the conditions studied here, the total uncertainty in k_s with the DGIC method is estimated to be 0.62% for carbon ions, 0.85% for the UHDR proton beam, and 2.36% for the UHDP electron beam. When compared with other methods, [162] reported a combined relative standard uncertainty for k_s on carbon ion beams of 0.36% using the Jaffé plot method. For UHDR proton beams, [177] estimated the uncertainty of the Jaffé plot method to be 0.2%; however, this estimate was addressed only under conventional dose rates and is therefore likely underestimated in the UHDR regime [177]. For UHDP electron beams, the reported uncertainties

vary depending on the method: dose comparison with water calorimetry yields an uncertainty of about 1.3% [26], while the Petersson semi-empirical model (for a specific chamber) indicates an uncertainty of 2.2% [150]. From this comparison, the DGIC method results in larger uncertainties in some cases. However, an important advantage is that it does not require additional measurements to determine k_s . As described in Appendix 5.A.3, the total uncertainty of the method is mainly influenced by the uncertainty in the measured current and the calibration of the detector. A promising way to significantly reduce this uncertainty would be to calibrate the device against a primary standard, such as a calorimeter, at the beam quality of interest. This approach may offer a practical compromise between time in clinical workflow efficiency and accuracy.

5.6 Conclusion

This work presents and validates a new method for correcting ion recombination based on a dual-gap ionization chamber design tailored for reference dosimetry. The method enables accurate determination of k_s in the top cavity from a single measurement, by exploiting the relationship between the collected charge between the two gaps. It has been demonstrated to be effective to correct for initial recombination in a carbon ion beam, a continuous UHDR proton beam, and, within a limited range, under a UHDP electron beam, offering a practical solution where conventional methods are less feasible to use due to the requirement of performing multiple measurements to assess k_s .

The DGIC method has been tested and remains valid to use up to 4.2 Gy per pulse, the limit of this study. Furthermore, while not yet explored in this study, the DGIC may be particularly well suited to UHDPP proton beams, where DPP values are generally lower than in electron beams. This represents a promising direction for future research.

Beyond recombination correction, the DGIC also provides dose rate estimates from a single acquisition, offering added value for quality assurance in UHDR and UHDP, where independent dose rate verification would be required.

Despite the limitations in extreme UHDP regimes, the DGIC method provides a practical alternative to conventional recombination correction techniques with ionization chambers. By enabling the determination of k_s from a single measurement, it reduces the complexity of deriving recombination losses and eliminates the need for multiple voltage acquisitions. The method's feasibility, along with its conceptual and experimental validation under the different conditions explored in this study, provides a solid basis for continued development and refinement.

5.A Supplementary derivations for the DGIC Method

5.A.1 Derivation of G-factor for initial recombination

Given Equation 2.21 for Jaffé theory for initial recombination for a specific plane parallel IC- i , with d_i distance between plates and V_i applied voltage:

$$f_i^{ini} = \frac{e^{-1/g}}{gq_i} [li(e^{1/g+ln(1+q_i)}) - li(e^{1/g})] \quad (5.9)$$

with:

$$g = \frac{\alpha N_0}{8\pi D_{\pm}}, \quad q_i = \frac{2d_i^2 D_{\pm}}{\mu_{\pm} b^2 V_i} \quad (5.10)$$

where the different constants have been defined in section 2.7.1, If a first order Taylor series expansion is performed around $q_i=0$, i.e., considering near saturation condition, the previous equation becomes:

$$f_i^{ini} \approx \frac{1}{1 + C_{ini} \frac{d_i^2}{V_i}}, \quad \text{where:} \quad C_{ini} = \frac{g D_{\pm}}{\mu_{\pm} b^2} \quad (5.11)$$

if $f = 1/k_s$, substituting M_T and M_B using the TRS-398 equation for reference dosimetry:

$$D_{w,Q} = (M_Q k_{T,P} k_s k_{pol}) N_{D,w,Q_0} k_{Q,Q_0} \quad (5.12)$$

and assuming no dose gradients are present and the dose measured in both gaps is the same, if $k_{T,P}^T = k_{T,P}^B$, $k_{pol}^i = 1$, Equation 5.1 becomes:

$$G = \frac{1 - \left(\frac{f_T}{f_B}\right)}{1 - f_T} \quad (5.13)$$

Substituting Equation 5.11 into 5.13, simplifies all dependencies on different parameters included in C_{ini} , allowing us to obtain G for initial recombination:

$$G_{initial} = 1 - \frac{d_B^2/V_B}{d_T^2/V_T} \quad (5.14)$$

5.A.2 Derivation of G-factor for volume recombination

Pulsed beams

According to Boag's theory, the collection efficiency when volume recombination of a plane parallel IC- i is present in a pulsed beam is:

$$f_i^{puls} = \frac{1}{u_i} \ln(1 + u_i) \quad \text{with} \quad u_i = \frac{2\alpha d_i^2 \bar{q}}{e\mu_{\pm} V_i} \quad (5.15)$$

where the different constants have been defined in section 2.7.2. If a Taylor series expansion is performed around $u_i=0$, the previous equation becomes:

$$f_i^{puls} \approx \frac{1}{1 + C_{puls} \frac{d_i^2}{V_i}}, \quad \text{where:} \quad C_{puls} = \frac{\alpha \bar{q}}{e\mu_{\pm}} \quad (5.16)$$

Similarly as in previous case, substituting 5.16 into 5.13 allows us to determine G for pulsed beams, which is the same expression as obtained for initial recombination:

$$G_{puls} = 1 - \frac{d_B^2/V_B}{d_T^2/V_T} \quad (5.17)$$

Continuous beams

According to Boag's theory, the collection efficiency when volume recombination of a plane parallel IC- i is present in a continuous beam is:

$$f_i^{cont} = \frac{2}{1 + \sqrt{1 + \frac{2}{3}\xi_i^2}} \quad \text{with} \quad \xi_i^2 = \frac{\alpha d^4 \bar{q}}{e\mu_{\pm}^2 V_i^2} \quad (5.18)$$

in which the different parameters have been defined previously in section 2.7.3. If a Taylor series expansion is performed around $\xi_i=0$, the previous equation becomes:

$$f_i^{cont} \approx \frac{1}{1 + C_{cont} \frac{d_i^4}{V_i^2}}, \quad \text{where:} \quad C_{cont} = \frac{\alpha \bar{q}}{e\mu_{\pm}} \quad (5.19)$$

substituting 5.19 into 5.13 allows us to determine G for continuous beams:

$$G_{cont} = 1 - \frac{d_B^4/V_B^2}{d_T^4/V_T^2} \quad (5.20)$$

5.A.3 Uncertainty on the DGIC method

All quoted uncertainties in this work are expressed as a standard uncertainty ($k=1$). The uncertainty associated with the DGIC inherent method was evaluated from the contributions from different parameters to the overall uncertainty on k_s , which arise from the following sources:

- Bias voltage: The electrometers used in this work provided highly stable bias voltage for each of the gaps (V_i , with $i=T,B$). With an estimated uncertainty in each voltage (u_{V_i}) of 1 V (type-B) and a nominal bias of 300 V for

both gaps, the relative uncertainty in the bias voltage ratio (u_{V_R}), obtained using Gaussian error propagation: $u_{V_R}^2 = \left(\frac{\partial V_R}{\partial V_T}\right)^2 u_{V_T}^2 + \left(\frac{\partial V_R}{\partial V_B}\right)^2 u_{V_B}^2$, is approximately 0.001%. At lower voltages the relative contribution is larger (e.g., 0.16% at 30 V).

- Air gap thickness: According to the methodology presented in earlier sections, the air-gap ratio can be obtained from the N_{D,w,Q_0}^i ratio of each of the gaps (i=T,B): $\frac{d_T}{d_B} = \frac{N_{D,w,Q_0}^T k_{Q,Q_0}^T}{N_{D,w,Q_0}^B k_{Q,Q_0}^B}$. However, because the uncertainty in each N_{D,w,Q_0}^i is typically 1%, the propagated uncertainty in the gap size ratio becomes unreasonably large. The alternative method described is therefore used, where the air gap size ratio can be obtained from: $\frac{d_T}{d_B} = \frac{M_T}{M_B} \frac{k_s^T \cdot k_{CM}^T}{k_s^B \cdot k_{CM}^B}$. Based on [164], the uncertainty in the product $k_s^i \cdot k_{CM}^i$ for each gap was taken as 0.3% (type-B). The type-A uncertainty in M_i , given by the standard deviation of the mean under ^{60}Co calibration, was 0.05%. The combined uncertainty in the air gap ratio (u_{d_R}) is obtained using gaussian error propagation of the previous variables: $u_{d_R}^2 = \left(\frac{\partial d_R}{\partial M_T}\right)^2 u_{M_T}^2 + \left(\frac{\partial d_R}{\partial M_B}\right)^2 u_{M_B}^2 + \left(\frac{\partial d_R}{\partial k_s^T \cdot k_{CM}^T}\right)^2 u_{k_s^T \cdot k_{CM}^T}^2 + \left(\frac{\partial d_R}{\partial k_s^B \cdot k_{CM}^B}\right)^2 u_{k_s^B \cdot k_{CM}^B}^2$. With this approach, u_{d_R} is 0.4%.
- Beam quality correction factors: The uncertainties in k_{Q,Q_0}^i for each gap were estimated as 0.4%, 0.7%, and 1.6% for electrons, protons, and carbon ions, respectively. These mainly stem from the uncertainty in $\bar{w}_{air}$. However, when taking the ratio k_{Q,Q_0}^R , the $\bar{w}_{air}$ terms cancel, reducing the relative uncertainty on the ratio of beam quality correction factors (u_{k_{Q,Q_0}^R}) to 0.6% for all particles. This value originates from a combination of type-A uncertainties over the dose values. Type-B uncertainties are also associated with MC calculations, primarily related to stopping power data, scattering data, and nuclear interaction data; however, since a ratio is calculated, these can be considered highly, if not fully, correlated.
- Collected charge: The uncertainty in the collected charge M_i arises from type-A uncertainty (standard deviation of the mean) under the experimental conditions being studied. In this work, the propagated uncertainty in the charge ratio (obtained from Gaussian error propagation as: $u_{M_R}^2 = \left(\frac{\partial M_R}{\partial M_T}\right)^2 u_{M_T}^2 + \left(\frac{\partial M_R}{\partial M_B}\right)^2 u_{M_B}^2$) was 0.07% for carbon, 0.7% for UHDR protons, and 1.5% for UHDP electrons, reflecting the higher output instabilities of some beams, especially in UHDR and UHDP conditions.

The total combined uncertainty in k_s is obtained by Gaussian propagation of the uncertainties from all sources, assumed to be independent from each other:

$$u_{k_s}^2 = \left(\frac{\partial k_s}{\partial V_R} \right)^2 u_{V_R}^2 + \left(\frac{\partial k_s}{\partial d_R} \right)^2 u_{d_R}^2 + \left(\frac{\partial k_s}{\partial k_{Q,Q_0}^R} \right)^2 u_{k_{Q,Q_0}^R}^2 + \left(\frac{\partial k_s}{\partial M_R} \right)^2 u_{M_R}^2$$

The largest contribution in the combined uncertainty arises from the ratio of the beam quality correction factors. As shown in Equation 5.7, k_{Q,Q_0}^R effectively reduces to the ratio of absorbed doses, which, for the very thin layer of material, is effectively the same. One way to reduce the associated uncertainty is to directly determine the air-gap size with the method described in the beam of interest (in which k_{Q,Q_0}^R is no longer needed). Considering the thin material layer between both air cavities and the use of the detector in conditions without significant dose gradients, a reasonable assumption is that the DGIC method is beam quality independent.

With this assumption, the overall uncertainty in k_s estimated with the DGIC method is approximately 0.62% for carbon ions, 0.85% for the UHDR proton beam, and 2.26% for the UHDP electron beam. The main contributions on uncertainty come from the standard deviation of the ratio of collected charges, which depends on detector design and on beam output stability.

Chapter 6

Discussion, conclusion and outlook

The past three chapters have described the core work of this thesis, namely the development of a simulation tool to model ion recombination efficiencies beyond the limits of existing theoretical models, a systematic study of the radiation tolerance of materials typically used for the construction of dosimetry devices under prolonged UHDR operation and a detailed investigation of a novel dual gap ionization chamber (DGIC) concept for reference dosimetry including its inherent method to correct for recombination losses. In the present chapter, we aim to re-contextualize these developments, discussing their potential practical implications as well as the associated challenges that may motivate further studies.

Advanced radiotherapy modalities, such as particle therapy and FLASH radiotherapy, require the development of new technologies to ensure that their highly complex delivery systems operate with the required accuracy and reliability.

For UHDR conditions, promising detector technologies such as silicon carbide diodes, diamond detectors or miniature calorimeters have emerged. While offering a reduced or, in some cases, no dependence on dose rate, they currently lack standardized calibration protocols, some of them unknown LET dependence in particle beams, long term stability data, and clinical familiarity. Introducing a new detector type implies new calibration protocols, QA procedures, regulatory validation, etc., which take years to standardize.

Despite the severe charge recombination effects that arise at UHDR and reduce charge collection efficiency, ionization chambers remain used for dosimetry research and development. This continued interest is primarily due to their established role as the reference instrument within the international dosimetry chain, providing robust traceability to primary standards. The physical behavior of ionization chambers is exceptionally well characterized, supported by decades of theoretical modeling, experimental data, and established correction methodologies.

Traditionally, to correct for ion recombination losses, correction methods rely on the assumed linear relationship between the inverse of collected charge and the inverse of applied voltage (or inverse square of the applied voltage for quasi-continuous beams). However, in advanced beam modalities, these methods become limited or impractical, as they often require complex procedures involving multiple measurements. To overcome these limitations, this thesis introduces a novel ionization chamber design for reference dosimetry. Its inherent operating principle overcomes the dependence on the conventional linearity requirement and eliminates the need for separate measurements to determine the ion recombination correction factor.

This thesis advances the understanding of ion recombination in ionization chambers by combining theoretical, computational, and experimental approaches. The dedicated Monte Carlo simulation developed in this work includes the interplay of multiple physical effects beyond conventional theoretical frameworks, providing a more comprehensive description of charge transport dynamics and recombination processes. The material study provides direct insight into the effects of the large cumulative doses delivered to dosimetric devices under prolonged UHDR exposure. It investigates the resulting changes in material properties and assesses their suitability for use in UHDR dosimetric applications. Finally, the design and development of the double gap ionization chamber (DGIC) demonstrate a pragmatic

approach to correct for recombination effects, a relevant effect in the context of advanced beam modalities.

The feasibility of the DGIC concept has been demonstrated through three principal contributions:

- As of September 2021, only a limited number of simulation tools existed to investigate recombination losses in ionization chambers, most of which relied on solving partial differential equations (PDE) that describe the evolution of charge carrier densities within the active volume of ionization chambers. Due to the potential limitations inherent to this approach, such as convergence issues in three dimensions, which are required to model recombination in particle beams, an alternative simulation framework was developed based on the Monte Carlo algorithm proposed in [63]. However, this approach was originally restricted to one dimension for plane-parallel geometry, and accounted only for drift and ion recombination as transport effects. To address these limitations, we developed a similar open source simulation tool, implemented in Python, that extends the approach to three dimensions for the plane-parallel geometry. In addition to drift and recombination, further transport mechanisms such as diffusion, free electron fraction and space charge screening were incorporated. The code was validated against experimental data across different particle beams and beam time structures, successfully reproducing the ion recombination correction factor for initial recombination, volume recombination in both continuous and pulsed beams at conventional dose rates, as well as their combined contributions.
- Radiation damage to dosimetric devices has been increasingly reported in recent years during experiments under UHDR conditions, raising concerns about the long term reliability of ionization chambers and quality assurance devices used for reference dosimetry. This motivated the second major contribution of this thesis: identifying and characterizing materials suitable for IC construction that can withstand prolonged UHDR exposure. This study was conducted in collaboration with Germany's national metrology institute, Physikalisch Technische Bundesanstalt (PTB), which had previously initiated similar investigations with electron beams. Since the objective of our work was to study the use of materials of ICs in particle beams, it was essential to extend the evaluation to protons. Candidate materials commonly used in ICs were selected, with PTB providing the corresponding samples for phantoms and preliminary testing under electron UHDR irradiation. These initial experiments, performed across a wide range of cumulative doses and dose rate conditions, established a reference framework for subsequent ex-

periments with proton beams, where beam time availability was much more limited. In the proton studies, UHDR irradiations were delivered to different samples to assess the effects of high cumulative doses, variable average dose rates, and different dose per pulse conditions. A broad set of material properties was systematically evaluated. Experimental results showed that irradiation induced visible and structural degradation in several materials, with damage primarily caused by total dose. No clear dependence on dose rate was observed, although extended high dose rate sometimes led to localized thermal effects. PEEK and graphite remained stable, confirming their suitability for UHDR applications. Interestingly, “healing effects” were observed in some materials, indicating partial recovery from radiation-induced damage. This investigation led to the identification of promising candidate materials for different dosimetric applications under UHDR irradiation. These findings directly influenced the material selection for the development of the DGIC prototype presented in this thesis.

- The third major contribution of this thesis was the development of a prototype DGIC, designed on the basis of the insights gained from the previous studies and carried out in close collaboration with IBA Dosimetry. The design aimed to achieve an optimal balance between charge multiplication and recombination losses, which was achieved with air gap sizes of 1.0 mm and 0.6 mm. Additionally, an adaptation of the original method described in [153] for reference dosimetry was derived. For the construction materials, PEEK was selected for insulating components and graphite for conductive elements. Through successive design iterations, a functional prototype was built and subsequently tested across a broad range of irradiation conditions. The chamber was calibrated with a ^{60}Co source, initial recombination was studied using a carbon ion beam, and volume recombination was characterized under a continuous UHDR proton beam. Although primarily intended for heavy-particle beams, the DGIC was also evaluated under an UHDP electron beam. In all experiments, the detector operated successfully, demonstrating the feasibility of the DGIC concept for reference dosimetry in advanced radiotherapy modalities.

The following subsections discuss the limitations of this work, outline future prospects for further development, and situate these findings within the broader context of advanced radiotherapy modalities and their associated challenges.

Simulation tools modeling ion recombination: limitations and perspectives

After demonstrating consistency with established theoretical models and experimental data at conventional dose rates, efforts were made to extend the validation of the Monte Carlo simulation tool to UHDR modalities. At this time, however, the availability of experimental datasets is limited, particularly for proton beams which are of main interest to this thesis. A preliminary study exploring the sensitivity of the simulation tool to a broad range of parameterizations for the constants governing ion transport revealed substantial variability, resulting in large uncertainties in the simulated ion recombination correction factor k_s under UHDR conditions (e.g., a combined uncertainty of $\sim 10\%$ was found for a 1 mm gap operated at 500 V, compared to $\sim 1\%$ at conventional dose rates). These considerations, together with the findings of Bourgouin et al. [29], which reported during experiments a dependence of k_s on air density, temperature and pressure, highlighted the difficulty of validating simulation tools without systematically controlled experimental datasets that monitor relevant ambient conditions.

Further progress in simulating k_s requires deeper knowledge and more comprehensive modeling of ion transport processes. Key challenges include:

- Limited availability of ion transport parameters data with explicit dependencies on ambient conditions.
- The influence of space charge screening and its interplay with other effects. Space charge screening effects perturbate the effective electric field experienced by ions, which in turn may affect other processes such as the free electron fraction and even affect transport parameters. For example, the ion recombination coefficient α , often treated as a constant, depends on both the ion-ion interaction cross section and the relative ion velocities, the latter being electric field dependent. Furthermore, space charge effects alter not only the electric field along the collection direction but also the radial component, potentially disrupting equilibrium near chamber edges and creating lateral imbalances.
- Charge multiplication effects, which become significant in small gap chambers yet remain poorly modeled, as further discussed in Appendix A. This effect depends strongly on both the air gap size and the applied voltage. For example, in an ionization chamber with a 0.6 mm gap operated at 500 V, charge multiplication can amount to approximately 1.5%. Such contributions are already relevant at conventional dose rates, and their interplay with other effects under UHDR conditions remains unknown.

In the dosimetry field, to simulate ion collection efficiencies, partial differential equation (PDE) based approaches are widely explored in the literature. These simulations evolve charge carrier densities undergoing different transport effects. They are deterministic, computationally efficient, and are particularly well suited for one-dimensional problems, such as parallel plate geometries. They reproduce average recombination losses accurately, but they may show some limitations: transport coefficients can only be treated as average values and their extension to higher dimensions or more complex geometries is restricted by meshing complexity.

In contrast, the Monte Carlo simulation developed in this work operates at the level of individual charge carriers. This provides maximum flexibility: stochastic fluctuations are naturally reproduced and complex geometries can be represented, allowing non-homogeneous distributions of ions (particularly relevant for high-LET beams). However, all this comes at a high computational cost, and the method still depends on general parametrizations since there is limited availability of data on interaction cross sections at low energies, which constrains the potential of this simulation approach.

Despite these limitations, simulation tools are essential for advancing the understanding of recombination processes beyond what is possible with theoretical models. Simulations enable investigation of the relative contributions of initial and volume recombination, exploration of intermediate regimes between continuous and pulsed irradiation, and to address a major research interest in the dosimetry field: predicting the charge collection efficiency of ionization chambers under extreme dose rates. Theories such as Jaffé's and Boag's involve assumptions that break down under UHDR conditions.

Nevertheless, it must be emphasized that simulation tools cannot replace measurements. Experimental conditions have a strong impact on the parameters required as model inputs, and these dependencies are particularly critical in UHDR, as discussed earlier. For this reason, simulations should be regarded as a complement to measurements: they are highly useful for predicting chamber behavior, supporting research, and guiding chamber design, but experimental methods remain indispensable for clinical reference dosimetry.

Long term reliability of QA devices under prolonged UHDR irradiation

Not only ionization chambers, but also several alternative active dosimeter concepts are currently being explored for FLASH applications, including silicon carbide detectors, graphite calorimeters, and miniaturized calorimeter probes. While these efforts are promising, a critical issue remains largely unaddressed in the literature:

radiation resistance and detector longevity under prolonged UHDR irradiation. For clinical transfer, dosimeters must not only provide accurate and reproducible responses at UHDR but also remain stable over extended periods of use.

Ionization chambers exemplify this challenge. They are indispensable as reference instruments in dosimetry protocols, where their reliability is essential for commissioning, beam characterization, and quality assurance. Yet, cases of ionization chambers breaking down after prolonged UHDR irradiation have been reported. Under such conditions, detectors can accumulate very high doses in short operational times, raising concerns about material degradation, calibration drift, and long-term response stability. This issue becomes particularly critical when considering the very high cumulative doses easily achievable when the detector may be exposed to prolonged UHDR. An example of this potential issue can be found in some quality assurance procedures, such as repeated PDD or beam profile measurements, where detectors may receive substantially higher cumulative doses within the same acquisition period than in conventional dose rates. In our experiments, for instance, doses exceeding 1 MGy were reached after only about 40 minutes of continuous irradiation, illustrating that such dose levels are not unrealistic in practical UHDR settings. While routine clinical workflows would be subject to radiation protection constraints that limit irradiation times, situations requiring prolonged acquisitions may still arise during commissioning or research, making the potential for high cumulative doses an important consideration.

To ensure clinical applicability, future developments in FLASH dosimetry must explicitly evaluate detector radiation resistance under conditions that closely replicate practical use. Our study focused on materials in isolation, providing valuable insights, but internal stresses in assembled detectors could still introduce unexpected failures. Moreover, the doses delivered in our experiments were very high and concentrated over short timescales, which may not fully capture real world use. Recovery effects occurring between irradiations, for example, could extend operational lifetimes beyond what our data suggest.

In summary, while considerable progress has been made in demonstrating the feasibility of detectors at UHDR for investigating the FLASH effect, their long-term durability remains an open issue. Addressing this challenge is essential for moving beyond proof of concept demonstrations toward clinically reliable reference tools, comparable in robustness to ionization chambers in conventional radiotherapy.

The DGIC concept and potential applications

As discussed throughout this thesis, experimental methods to determine ion recombination correction factors in ionization chambers can become particularly complex in advanced beam modalities. Recent recommendations, for instance, discourage the use of the two voltage method and emphasize instead the study of the full Jaffé plot. Special care is required in certain beams and for ionization chambers with small air gaps, where charge multiplication effects become significant. In carbon ion beams, for example, extrapolation of the full curve is not straightforward and the choice of voltages is critical, since the Jaffé plot is nonlinear. At higher voltages, charge multiplication may overlap with the recombination curve (see Figures 2.17 and 2.18), leading to incorrect determination of the saturation current and, ultimately, underestimation of the recombination correction factor. The challenge with experimental methods is even greater in UHDR/UHDP modalities, where conventional correction methods often fail or require multiple measurements under varying conditions, an impractical approach for clinical workflows.

The double gap ionization chamber (DGIC) offers a potential solution to these issues. Because charge is measured simultaneously in both gaps, no additional measurement is required to determine recombination, and no voltage variation is needed. This simplifies operation and removes the complications associated with studying the linear regions of Jaffé plots. In terms of uncertainty, the DGIC introduces slightly higher values than conventional methods. However, this drawback is offset by the ease of use. Moreover, if calibrated against a primary standard in the beam quality under study, the dominant source of uncertainty, arising from calibration, can be significantly reduced.

The DGIC was primarily conceived for particle beams, where it has shown promising performance. However, when tested under the more extreme conditions of UHDP electron beams, the response saturated after 1.2 Gy per pulse, a limitation partly attributable to the electrometers employed. Further evaluation with more advanced electrometers is needed. Also, its usability might be extended by operating at higher voltages or using smaller gaps, though such modifications introduce new challenges in achieving the required tolerances with sufficient precision. In any case, for the clinical translation of FLASH aimed at treating deep-seated tumors, proton beams will likely be used. In such cases, instantaneous dose rates are less extreme, and the DGIC concept remains fully applicable.

In recent years, alternative strategies have been proposed to mitigate recombination with ionization chambers, such as reducing the gap size or using gases that

minimize electron attachment. While such approaches can reduce or eliminate the need for recombination corrections, valuable information can no longer be extracted from recombination. Since initial and volume recombination are inherently related to LET and dose rate, respectively, retaining some sensitivity to these effects is advantageous. With the DGIC, this becomes possible. As described in Chapter 5, the dual gap concept could even be extended to large area ionization chambers (LAICs) used for determining integrated depth dose curves in particle beams. With appropriate tuning, such design could also provide LET information. A major challenge for this application, however, lies in the relative large gap size needed to have sensitivity on recombination with LET and the difficulty of ensuring full parallelism across both gaps, which is an issue already present in conventional LAICs. Other uses, such as dose rate beam monitoring at UHDR with the ICs in the nozzle, are equally promising.

Although the current DGIC remains a prototype, requiring refinements such as reduced external dimensions, improved insulation, and mitigating occasional instabilities, it provides a strong foundation for future development. The results demonstrate that the DGIC and its potential variants and applications represent a promising approach to reliable dosimetry in advanced radiotherapy modalities.

Final considerations

Novel radiotherapy techniques require equally novel dosimetric tools to accompany their development. As treatment modalities such as FLASH radiotherapy and high-LET particle therapy advance, it is indispensable that dosimetry evolves in parallel to ensure accuracy, safety, and reliability.

Ion recombination is only one of many processes that affect ionization chamber performance, yet it plays a critical role in reference dosimetry for advanced beam modalities. The work presented in this thesis contributes to this field by developing a new simulation approach, characterizing materials that can withstand prolonged UHDR irradiations, and introducing the double gap ionization chamber (DGIC) concept. Together, these efforts demonstrate pathways toward simpler and faster reference dosimetry compared with conventional chamber designs. They also highlight the potential of unconventional detector architectures that can extract additional beam information, such as LET and dose rate, for improved quality assurance in advanced beam modalities.

While significant progress has been made in recent years, many challenges remain. In UHDR applications, systematic studies of detector longevity and radiation resistance are still scarce, though they are crucial for ensuring stable reference

instruments. Simulations continue to face limitations in parameterization and validation, especially at clinically relevant UHDR beam conditions, highlighting the need for comprehensive experimental datasets. The DGIC, although still at the prototype stage, has demonstrated feasibility and versatility, but further refinements in design and manufacturing are required.

The clinical translation of FLASH proton therapy is still at an early stage, with many aspects requiring clarification before routine use can be considered. A clearer understanding of the biological mechanisms underlying the FLASH effect, together with precise characterization of the beam parameters required to trigger it, will be essential for safe and reproducible implementation. Beyond the FLASH effect itself, UHDR irradiation may offer several practical clinical advantages. The extremely short beam-on times achievable at UHDR could reduce the impact of organ motion and mitigate interplay effects in particle therapy, thereby improving the accuracy of dose delivery without relying as heavily on motion management strategies or robust optimization. In addition, the potential to deliver effective treatments in only a few large fractions (hypofractionation) would shorten treatment schedules and reduce the number of hospital visits, improving both patient convenience and healthcare efficiency. Another hypothesized consideration is the reduced irradiation of circulating blood volume with UHDR, which could spare immune cells from radiation damage. Preserving immune competence may enhance the repair of normal tissues and improve overall treatment outcome.

High-LET particle therapies, such as carbon ions and other heavy-ion treatments, are already clinically available in several centers worldwide. By combining highly conformal dose distributions with an elevated relative biological effectiveness, they offer particular promise for the treatment of radioresistant tumors. Ongoing studies are expanding the clinical evidence base, but broader adoption will depend on continued technological innovation and rigorous clinical validation. As the technology matures, high-LET therapy could complement existing photon and proton modalities, thereby broadening the therapeutic options available to patients.

The combined challenges of high-LET treatments and UHDR irradiation highlight the need for further detector innovation and robust, practical dosimetric tools. The developments presented in this thesis: novel simulation strategies, material studies, and the DGIC prototype, provide a foundation for addressing these challenges. Strengthening reference dosimetry in these demanding scenarios will be essential to enable the safe clinical adoption of emerging radiotherapy modalities.

Appendix A

Experimental study on charge multiplication

This appendix provides experimental insight into the charge multiplication correction factor with the main goal of further understanding of how the parameter γ depends on different parameters, complementing earlier hypotheses proposed in the literature. The work was carried out in collaboration with IBA, who designed and manufactured modified PPIC prototypes to enable a systematic study of electrode gap dependence, and was experimentally tested at the Radiation Physics Laboratory of the University of Santiago de Compostela (USC), Spain. The measurements, performed under controlled variations of gas pressure, composition, and chamber geometry, provide an exploratory dataset that broadens the characterization of charge multiplication effects. What follows is a brief overview of the main results underlying this work.

Summary

Objective: This study aimed to investigate the dependence of the charge multiplication correction factor k_{CM} and its associated parameter γ on chamber geometry, polarity, atmospheric pressure, and gas composition. Particular focus was placed on testing the hypothesis that γ depends on electrode spacing, as previously suggested in the literature, using modified plane-parallel ionization chambers (PPIC) prototypes manufactured by IBA.

Approach: Two chamber models, PPC05 and PPC40, were modified to obtain different electrode gaps while preserving electrode radius. The prototypes were characterized with X-ray micro-CT imaging and subsequently tested at the Radiation Physics Laboratory of the University of Santiago de Compostela (USC), Spain, using both an X-ray tube and a ^{60}Co beam. Measurements were performed under controlled atmospheric conditions (air and N_2 , pressures from 100–1100 hPa) with both positive and negative polarities, in floated and grounded input configurations. Saturation curves and Jaffé plots were obtained and fitted to extract γ and k_{CM} .

Main results: Within the recommended operating pressure range (900–1100 hPa), atmospheric pressure and gas composition had negligible influence on charge multiplication, whereas strong effects were observed at 100 hPa, particularly with air versus N_2 . Polarity effects were generally consistent across prototypes, except for the PPC05 with a 2.6 mm gap, where an insufficient guard ring width led to elevated k_{pol} . A clear dependence of γ on electrode spacing was confirmed, with approximately linear trends for PPC40-type chambers. Differences between chamber types for the same electrode spacing could not be attributed to active volume effects alone.

Significance: The findings support the dependence of γ on electrode spacing and highlight limitations of current models based solely on tabulated Townsend coefficients, which fail to reproduce the experimental data. While the work strengthens the evidence for geometry-driven charge multiplication effects in PPICs, further studies with different detectors and theoretical refinements are required to establish reliable predictive models for dosimetry.

A.1 Motivation

The dependence of the constant γ in Equation 2.68 on various parameters remains insufficiently understood. Rossomme et al., [164] provided first steps by hypothesizing a dependence of γ on the air gap size, opening the way for further investigation. In particular, the influence of atmospheric pressure, gas composition, and chamber geometry on γ has not yet been systematically explored.

To contribute to this line of research, this appendix presents an experimental study of the charge multiplication correction factor k_{CM} and its associated parameter γ :

$$k_{CM} = e^{-\gamma \cdot V} \quad (\text{A.1})$$

where V denotes the magnitude of the applied voltage (in V) and consequently, the parameter γ has units of V^{-1} .

The experimental analysis in this study includes Jaffé plots under varying conditions of pressure, gas mixtures, and chamber geometries. IBA designed and manufactured a set of PPIC prototypes of existing designs with modified air gap sizes, enabling a controlled investigation of the geometry of their PPICs on charge multiplication.

A.2 Materials and Methods

Two chamber models from IBA were employed: PPC40 and PPC05. For the PPC05-type chambers, the electrode gap was adjusted to 0.6 (nominal value, SN 1784), 1.2 and 2.6 mm, while preserving the original electrode radius of 4.95 mm. This resulted in chamber volumes ranging 46 - 220 mm³. For the PPC40-type chambers, the electrode gap was modified to 1.0, 1.5 and 2.0 mm (nominal value, SN 1331), with the original electrode radius of 8 mm maintained. The corresponding chamber volumes ranged 201 - 402 mm³. Verification of the modified electrode gaps was performed using X-ray micro-CT imaging (*Bruker Skyscan 1272*).

Prototype chambers were subsequently tested at the Radiation Physics Laboratory of the University of Santiago de Compostela (USC), Spain, using both an X-ray tube and a ⁶⁰Co beam. Measurements were conducted within an in-house developed vacuum system, where pressure was carefully monitored and regulated with an electrovalve, allowing to keep the desired pressure within variations of ± 1 hPa. For the nominal PPC40 chamber, tests were performed in both air and nitrogen (N_2) at pressures of 1000 (standard), 500 and 100 hPa. N_2 measurements were included to assess the potential influence of recombination on the Jaffé plots,

while pressure variation was used to explore charge multiplication behavior and its relation to the Townsend coefficient, which is expected to depend on atmospheric pressure.

For the remaining prototypes, tests with ^{60}Co were conducted in air at standard pressure (1000 hPa), and added limited values of $\pm 10\%$ (900–1100 hPa), corresponding to the recommended operating pressure range for ionization chambers.

Saturation curves (collected charge M versus applied voltage V) and Jaffé plots (inverse charge $1/M$ versus inverse voltage $1/V$) were obtained for polarizing voltages between 25 V and 500 V, for both negative and positive polarities, and in floated and grounded input modes. In the floated input mode, the outer chamber wall is held at ground potential while the collecting electrode is biased. In the grounded input mode, the electrometer amplifier is held at ground potential, providing the bias to the polarizing electrode. A schematic representation of both configurations is shown in Figure A.1. In this work, the floated input mode is used by default unless otherwise specified.

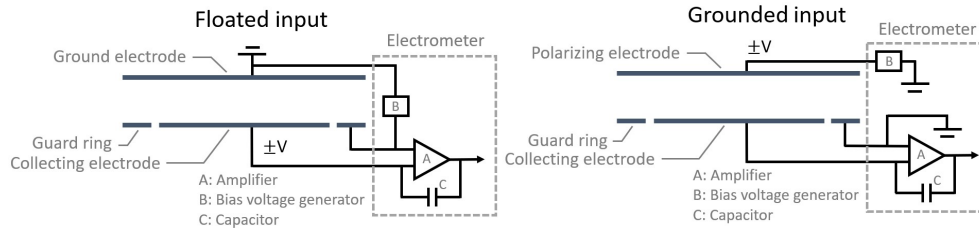


Figure A.1: Schematics of floated input (left) and grounded input (right) configurations. Adapted from [80] for plane-parallel geometry.

For clarity, both saturation curves and Jaffé plots are presented throughout the results section, as they provide complementary perspectives that may facilitate interpretation of the results. Data were normalized to the saturation current, determined from extrapolation at the lowest voltages (25–100 V), following the recommendations of [68].

A.3 Results

A.3.1 Electrode distance

Table A.1 summarizes the electrode gaps measured for the modified PPIC prototypes using micro-CT imaging. The measured values agree closely with the intended modifications.

PPIC	Electrode distance (mm)
PPC05 - 0.6*	0.59 ± 0.03
PPC05 - 1.2	1.19 ± 0.02
PPC05 - 2.5	2.73 ± 0.02
PPC40 - 1.0	1.03 ± 0.03
PPC40 - 1.5	1.48 ± 0.04
PPC40 - 2.0*	1.96 ± 0.02

Table A.1: Measured electrode distances of the PPIC prototypes. Superscript * indicates the nominal air gap size of the original commercial detector by IBA.

A.3.2 Influence of atmospheric pressure and gas composition

Figure A.2 shows the saturation curve and the corresponding Jaffé plot (left and right, respectively), normalized to the saturation current, for PPC05 chambers irradiated with a ^{60}Co beam at atmospheric pressures between 900 and 1100 hPa in air.

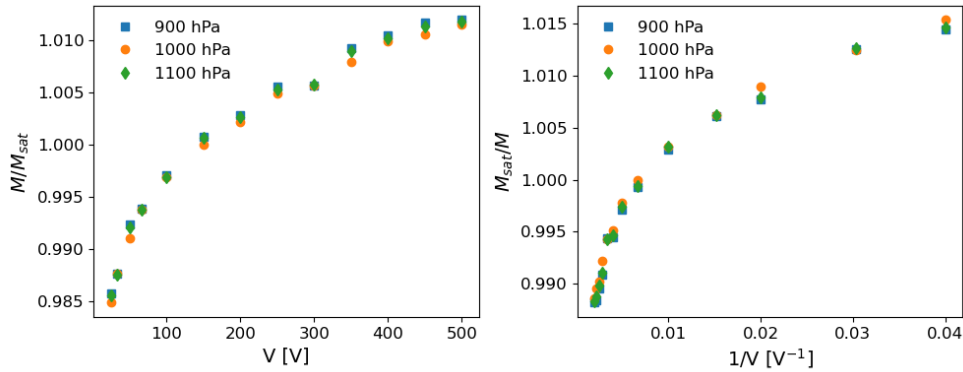


Figure A.2: Saturation curve (left) and Jaffé plot (right) for a PPC05 with nominal air gap at maximum and minimum recommended pressures.

Figure A.3 presents the corresponding results for a PPC40 under X-ray tube, for pressures of 100, 500 and 1000 hPa, in both air and N_2 . At low pressure (500 hPa), the PPC05 experienced electrical arc due to its small electrode gap and could not be measured under these conditions. The PPC40 results show that the curves at 500 hPa and 1000 hPa are nearly identical, while the response at 100 hPa differed significantly. Furthermore, replacing air with N_2 at 100 hPa reduced the effect of charge multiplication.

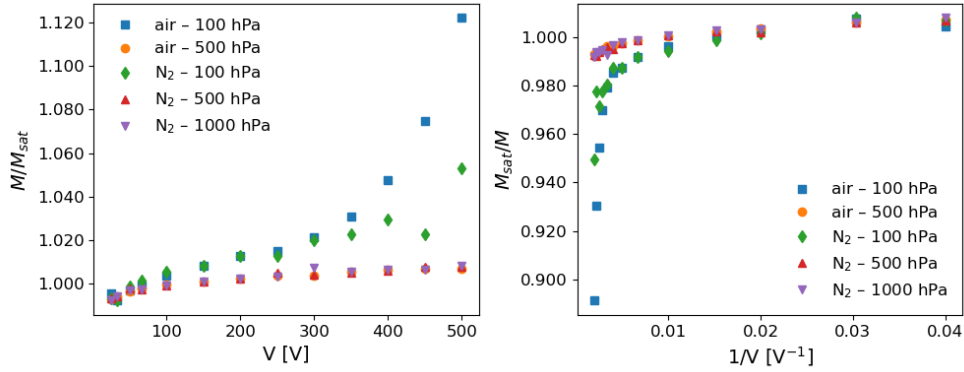


Figure A.3: Saturation curve (left) and Jaffé plot (right) for a PPC40 at pressures of 100–1000 hPa in air and N_2 .

Overall, these results indicate that moderate variations in pressure (within the 500–1000 hPa range) and changes in gas composition have little effect on the saturation curves. Therefore, the following analyses are restricted to measurements performed in air at standard pressure (1000 hPa).

A.3.3 Influence of positive, negative and inverse polarity

Figure A.4 shows the Jaffé plots for PPC05-type (left) and PPC40-type (right) prototypes operated under positive and negative polarities, with both floated and grounded input configurations measured under a ^{60}Co beam. When the direction of the electric field was the same (e.g. positive polarity with grounded input and negative polarity with floated input), the Jaffé plot curves are identical.

Figure A.5 presents the polarity correction factors k_{pol} obtained under floated input conditions. Similar trends are observed across all prototypes, with the exception of the PPC05-type chamber with a 2.6 mm gap, which exhibits systematically higher k_{pol} values, particularly at lower voltages. This behavior can likely be attributed to the insufficient guard ring width, which was not adapted when the electrode gap was enlarged beyond the nominal design. According to IAEA TRS-398 [78], the guard ring width should be at least 1.5 times the electrode spacing. With the exception of the PPC05-type 2.6 mm prototype, all investigated chambers satisfy this condition.

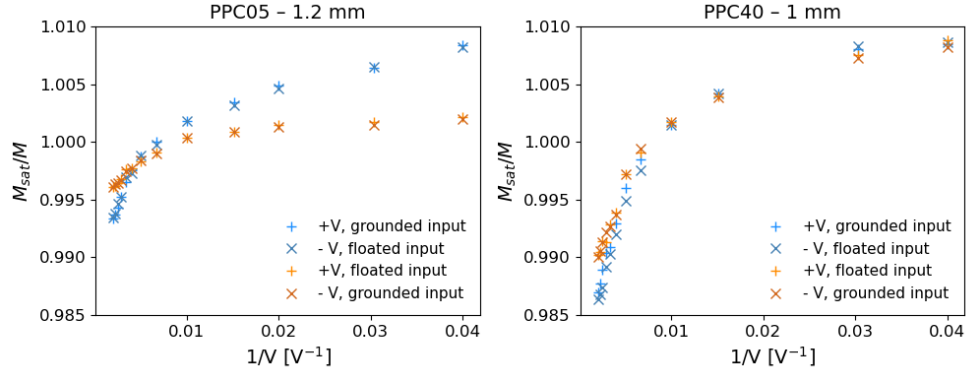


Figure A.4: Jaffé plots for PPC05 and PPC40-type prototypes with similar electrode gaps (~ 1 mm), comparing positive and negative polarities under grounded and floated input modes.

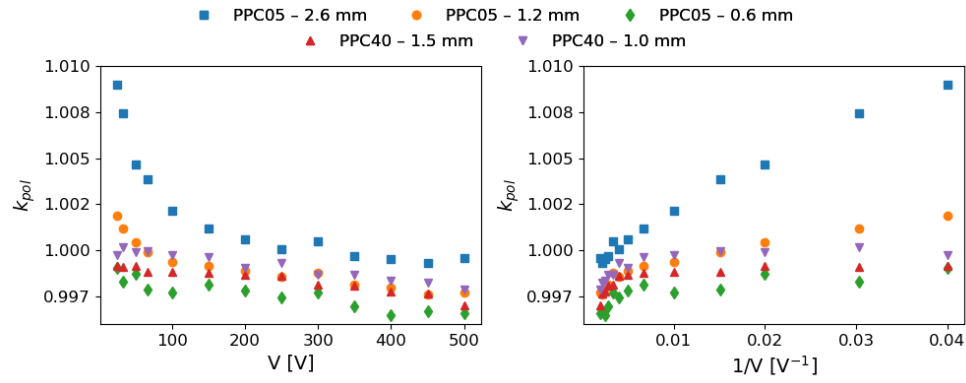


Figure A.5: Polarity correction factor k_{pol} as a function of the applied voltage (left) and of the inverse voltage (right) for the different PPIC prototypes.

A.3.4 Dependences on chamber geometry

Figure A.6 shows the parameter γ , obtained by fitting the exponential expression 2.68 to the Jaffé plots of the floated input curves, as a function of the measured electrode gap grouped by detector type and polarity. For a given chamber geometry and polarity, specifically for PPC40-type, the results exhibit an approximately linear dependence. For nominal PPC05 and PPC40 extra data points (in total three and two, respectively) from additional chambers were added, and lied within expected trend. Figure A.6 (c) shows the charge multiplication correction factor for the different chambers in this study.

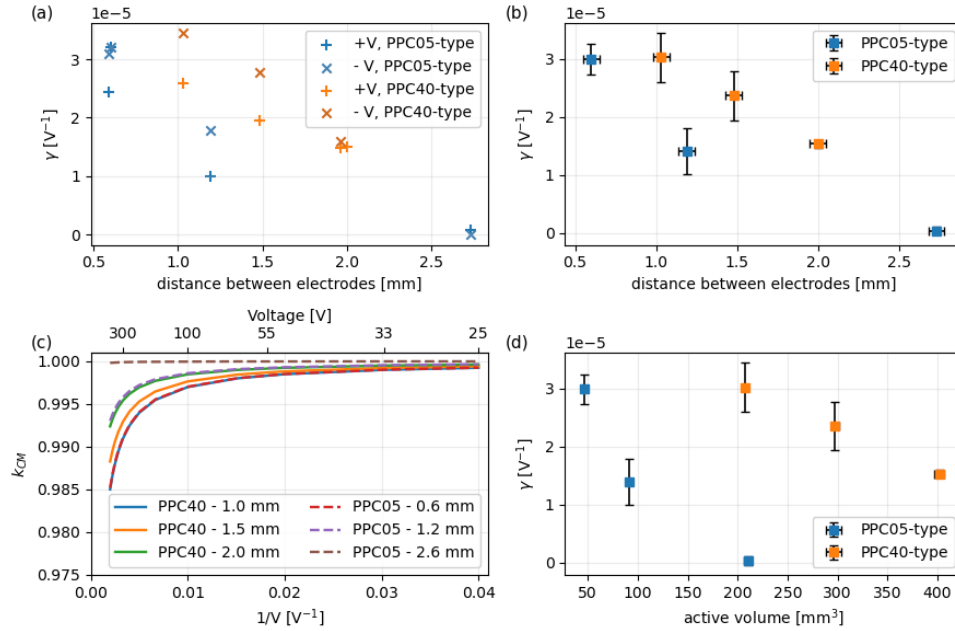


Figure A.6: Parameter γ from Equation 2.68: (a) as a function of electrode spacing for different polarities and chamber types, (b) averaged over both polarities as a function of electrode spacing, (c) charge multiplication correction factor averaged over both polarities for all detectors investigated, and (d) averaged over both polarities as a function of the active volume.

A.4 Discussion and conclusion

The present study investigated the dependence of the charge multiplication correction factor k_{CM} and its associated parameter γ on pressure, gas composition, polarity, and chamber geometry using modified PPIC prototypes.

First, the influence of atmospheric pressure and gas composition was examined. Within the extremes of range recommended (900–1100 hPa), no significant effect was observed on the saturation or Jaffé plots. At very low pressures (100 hPa), however, charge multiplication increased significantly, consistent with the expected dependence of the Townsend coefficient on pressure. Substituting air with N_2 at 100 hPa further reduced charge multiplication. This experimental observation can be attributed to the absence of oxygen-driven attachment–detachment processes. In air, oxygen contributes to both electron attachment and detachment pathways, particularly through detachment involving N_2 , which increases the effective Townsend ionization rate [143]. In N_2 , these mechanisms are suppressed, resulting in reduced charge multiplication.

The polarity correction factor k_{pol} followed similar behaviours for all detectors investigated with the exception of the PPC05-type prototype with a 2.6 mm gap, where higher k_{pol} values were attributed to an insufficient guard ring width. Jaffé plots were identical when the electric field direction was equivalent, independently if floated or grounded input was used.

A clear dependence of γ on electrode spacing was also identified, supporting the observation of [164]. For a given chamber type and polarity, γ exhibited an approximately linear decrease with increasing electrode gap. The PPC40 demonstrated larger γ values than the PPC05 for the same electrode spacing, a difference that could not be explained by variations in active volume, which showed a comparable trend. This suggests that additional geometrical factors, such as the radius of the collecting electrode (larger in the PPC40 than in the PPC05), may influence the parameter γ . Systematic studies with multiple detectors of comparable materials but varying electrode geometries and distances are therefore needed to fully characterize the geometrical dependence of this parameter.

The charge multiplication behavior observed in PPICs remains under discussion. While the Townsend coefficient is generally assumed to describe the charge multiplication correction factor, its applicability to air gap sizes operated at conventional voltages in radiotherapy ionization chambers has not been thoroughly validated. As illustrated in Figure A.7, the charge multiplication correction factors simulated with [147] from tabulated Townsend coefficients in air using Magboltz, would need to differ significantly in order to reproduce the experimental observations reported.

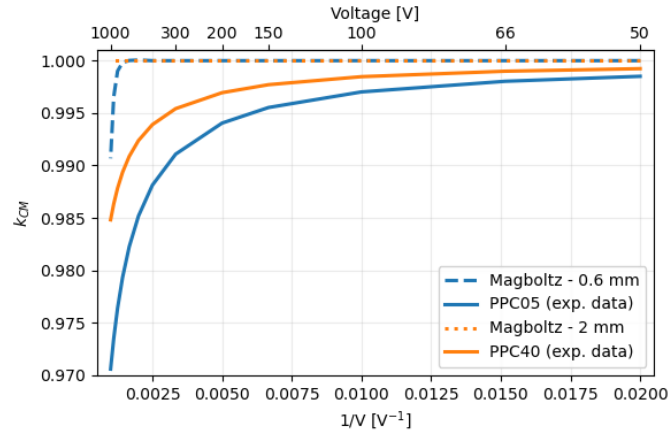


Figure A.7: k_{CM} values simulated (dashed lines) and compared with experimental data from this work (solid lines) for PPC40 (orange) and PPC05 (blue).

This discrepancy highlights the need for additional experimental and theoretical work by the scientific community to clarify the dependence of γ and to establish reliable models for practical dosimetric applications.

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