



UNIVERSITÀ
DEGLI STUDI
DI BRESCIA



Progetto Finanziato dall'Unione Europea – NextGenerationEU

DIPARTIMENTO DI INGEGNERIA MECCANICA E INDUSTRIALE

DOTTORATO DI RICERCA IN
INGEGNERIA MECCANICA E INDUSTRIALE
XXXVIII° CICLO

Tesi di Dottorato

Caratterizzazione ed Ottimizzazione del Processo Industriale di
Sterilizzazione con Radiazione Ionizzante

(Characterization and Optimization of the Industrial Sterilization Process with Ionizing Radiation)

Fisica Sperimentale (FIS/01)

Supervisore:

Chiar.mo Prof. Davide Pagano

Dottorando:

Lorenzo Sostero

Abstract

La sterilizzazione è un processo critico in ambito medico, poiché garantisce che i dispositivi medici siano privi di microrganismi e sicuri per l'uso sui pazienti. Tra le diverse tecniche di sterilizzazione, quelle che impiegano radiazioni ionizzanti hanno assunto un ruolo sempre più rilevante, poiché consentono tempi di trattamento ridotti, evitano l'esposizione dei prodotti ad alte temperature e non lasciano residui chimici al termine del processo.

Questo lavoro di tesi si concentra sulla sterilizzazione a fascio di elettroni, con applicazione specifica all'impianto industriale di Copan, aziende italiana produttrice di dispositivi medicali.

Nello specifico, sono state impiegate simulazioni Monte Carlo (utilizzando Geant4) per modellare la distribuzione della dose all'interno delle scatole di prodotti, consentendo di identificare strategie — come l'ottimizzazione dell'orientamento dei prodotti — per migliorare l'uniformità della dose. La quantificazione delle incertezze delle simulazioni ha ulteriormente rafforzato l'affidabilità dei risultati, fornendo linee guida per incrementare l'efficienza del processo mantenendo al contempo la qualità del prodotto.

Inoltre, è stato studiato in maniera sistematica l'impatto delle radiazioni ionizzanti sui polimeri utilizzati nella stampa 3D a deposizione di filamento fuso (FFF), data la loro crescente rilevanza anche nella produzione di dispositivi medici. Le analisi meccaniche, termiche e spettroscopiche hanno rivelato che il degrado indotto dalle radiazioni è dominato dalla scissione delle catene polimeriche, con effetti principalmente sulle proprietà meccaniche. Tra i materiali testati, il PLA ha mostrato la minore resistenza alle radiazioni, mentre TPE e ABS hanno dimostrato maggiore stabilità, mantenendo prestazioni meccaniche fino a dosi dell'ordine dei MGy.

Nel complesso, questo lavoro di tesi contribuisce a facilitare l'applicazione su scala industriale della sterilizzazione a elettroni e ad approfondire il comportamento dei polimeri esposti a radiazioni. Il modello di simulazione sviluppato e i risultati sperimentali forniscono strumenti pratici per l'ottimizzazione dei processi di sterilizzazione e per guidare la selezione dei materiali nei dispositivi medici sterilizzati con l'utilizzo di radiazioni, offrendo un valore diretto a Copan e, più in generale, al settore medico.

Abstract

Sterilization is a critical process in healthcare, ensuring that medical devices are free from viable microorganisms and safe for patient use. Among the available sterilization techniques, ionizing radiation has gained increasing importance due to its short treatment times, low operating temperatures, and absence of chemical residues. This thesis focuses on electron beam (e-beam) sterilization, with specific application to the industrial facility of Copan, a leading Italian manufacturer of medical devices.

Monte Carlo simulations (based on Geant4) were employed to model dose distributions within product boxes, and allowed the identification of strategies — such as optimized product orientation — to improve dose uniformity. Uncertainty quantification further strengthened the reliability of the results, providing guidelines for increasing process efficiency while maintaining product quality.

In addition, the impact of ionizing radiation on polymers used in Fused Filament Fabrication (FFF) 3D printing was systematically studied, given their growing relevance also in medical device manufacturing. Mechanical, thermal, and spectroscopic analysis revealed that radiation-induced degradation is dominated by chain scission, primarily affecting mechanical properties. Among the tested materials, PLA exhibited the lowest radiation tolerance, while TPE and ABS demonstrated higher stability, retaining mechanical performance up to doses in the MGy range.

Overall, this work contributes to facilitating the industrial-scale application of e-beam sterilization and to advancing the understanding of polymer behavior under radiation exposure. The developed simulation framework and experimental findings provide practical tools for optimizing sterilization processes and for guiding material selection in radiation-sterilized medical devices, offering direct value to Copan and to the wider healthcare manufacturing sector.

Table of Contents

	Page
Introduction	1
1 Sterilization Methods with Ionizing Radiations	3
1.1 Medical Device Sterilization Principles	3
1.2 Ethylene Oxide Sterilization (Chemical Method)	5
1.3 Radiation-Matter Interaction in Radiation Sterilization	8
1.4 Ionizing Radiation Sterilization (Overview)	15
1.4.1 Gamma Sterilization	17
1.4.2 Electron Sterilization	18
1.4.3 X-ray Sterilization	19
1.5 Dosimetry in Radiation Sterilization	20
1.5.1 Alanine Dosimeters	20
1.5.2 Radiochromic Dosimeters and CTA Strips	22
2 The Electron Sterilization Process in Copan	25
2.1 Rhodotron Accelerator	26
2.2 Copan Sterilization Plant	33
2.3 Dose Map Simulations Using Geant4	34
2.3.1 Dose Mapping Using Voxels	35
2.3.2 Dose Mapping Using Sensible Volumes	38
2.4 Dose Map Simulations Uncertainty	41
2.4.1 Statistical Uncertainty on Simulations	42
2.4.2 Systematic Effects on Simulations	45
2.5 Irradiation Setup Optimization	54
3 Radiation Effects on Polymers	61
3.1 Physics of Radiation Induced Effects on Polymer	62
3.2 Experimental Investigation on Polymers for 3D Printing	65
3.2.1 Sample Irradiation	65

TABLE OF CONTENTS

3.2.2	Tensile Test	67
3.2.3	Thermal Tests	72
3.2.4	Spectroscopy Tests	78
3.2.5	Analysis and Results	81
4	Conclusion	85
	Bibliography	87

Introduction

The sterilization is a fundamental process that guarantees that medical devices, pharmaceuticals, and other healthcare products are free of viable microorganism, to prevent patient exposure to infections or to a false diagnosis. Although basic methods of sterilization were already in use in the early 1900s [1], the practice has advanced greatly over the centuries, resulting in the highly effective techniques used in modern times. Among the various techniques available, those using ionizing radiation have gained increasing interest because of the short treatment time, the relatively low temperatures involved in the process, and the absence of chemical residuals after the treatment [2, 3].

This thesis focuses on electron beam sterilization, as implemented at Copan (Via F. Perotti 10, Brescia - Italy), an Italian company operating in the medical device manufacturing sector, which also co-founded this work in the context of the PNRR program, D.M. 352/2022. In particular, this research is motivated by the need of Copan to further characterize the e-beam sterilization process, that is of course the first step towards an optimization of the process, and to gain better understanding of the effect of ionizing radiations on polymers used in medical devices, since radiation can induce physical and chemical changes in polymers, potentially compromising product performance.

This work is organized as follows. The first chapter provides a comprehensive overview of sterilization methods with ionizing radiation. It begins with fundamental principles of medical device sterilization and then it describes the ethylene oxide sterilization process, one of the most common (chemical) sterilization technique. The chapter then introduces the physics of radiation-matter interaction, then it presents an overview on gamma rays, electrons, and X-rays sterilization techniques. The chapter concludes with a detailed discussion on dosimetry, a critical component of radiation sterilization validation, including common dosimeter technologies used in industry. The second chapter describes the electron beam sterilization plant at the

Copan facility, which utilizes a Rhodotron accelerator. Detailed characterization of the irradiation process is performed using Monte Carlo simulations (Geant4) to model dose distributions within products and packaging. This chapter also addresses uncertainty quantification and, finally, evaluates several methods for optimizing the irradiation setup to achieve uniform dose distribution inside the product. The third and final chapter explores the impact of ionizing radiation on polymers. More precisely, this chapter focuses on 3D printing materials for Fused Filament Fabrication (FFF), which are increasingly used also in the medical device manufacturing field. Experimental investigations were conducted on selected polymer samples, with analyses including mechanical testing, thermal analysis, and spectroscopic characterization. The irradiations were performed at the Hubert Curien Laboratory (LabHC) in Saint-Etienne (France), and sample characterizations were jointly performed at LabHC and at the Materials Science and Technology Laboratory (MaSTLab) of the University of Brescia (Italy). The collected data allow to compare the different materials analyzed, providing useful information for the selection of the most radiation tolerant ones.

Sterilization Methods with Ionizing Radiations

The sterilization of a medical product is a fundamental process that guarantees that the medical device is free of viable microorganism, to prevent patient exposure to infections or to a false diagnosis. International Standards specify the requirements for validation and routine control of sterilization processes: more precisely, the requirements for medical devices to be designated "sterile" are defined in the EN 556-1:2024, which defines a medical device as sterile only when a validated sterilization process has been conducted and its effectiveness is maintained under periodic monitoring. The following sections will provide an overview of the medical device sterilization principles and processes, with a focus on the ionizing radiation sterilization.

1.1 Medical Device Sterilization Principles

The sterilization procedure is intended to ensure that medical devices meet the necessary sterility assurance levels in order to minimize the risk of infection transmission and/or false response for diagnostic devices. The Sterility Assurance Level (SAL) quantifies the efficacy of inactivation, and it denotes the probability of a single viable microorganism surviving on an item following sterilization. SAL is a critical parameter that is employed to evaluate and validate sterilization procedures, as per ISO 11137, one of the international standards that regulate medical sterilization processes. The definition of the SAL also suggests that the inactivation of the microorganism is not deterministic, but it is described in terms of probability. More precisely, the probability that

a microorganism survives the sterilization process is described through an exponential decay function in time of sterilization treatment. For this reason, there is always a non-zero probability that certain microorganisms survive the sterilization procedure, despite the use of rigorous sterilization methods. This probability is influenced by a variety of factors, such as the environmental conditions in which sterilization is conducted, the physical and chemical properties of the sterilizing agent, and the inherent resistance of various microbial species. Typical values for SAL are established at 10^{-6} and 10^{-3} in order to quantify sterility assurance. A SAL of 10^{-6} suggests that the probability of a viable microorganism remaining on the sterilized product is one in a million, thereby ensuring a high level of sterility. Conversely, a SAL of 10^{-3} is generally regarded as less stringent, as it corresponds to a probability of one in a thousand. The selection of the appropriate SAL is contingent upon the intended use of the medical device and the potential repercussions of contamination. In order to guarantee the highest safety standards, critical devices, including surgical instruments and implants, typically necessitate a SAL of 10^{-6} . Conversely, products with reduced sterility risks may be acceptable with a SAL of 10^{-3} .

Other than reaching the desired sterilization level, an ideal sterilization process should guarantee the following requirements:

- The sterilization process should not induce damage on the products.
- The sterilization process should be able to quickly treat high volumes of products.
- Sterilization should be achieved for any products and packaging, independently of the material, the geometry, the density, etc.
- The sterilization agent should not remain as a residual in the products at the end of the sterilization process.
- The sterilization process should guarantee that the products are free of amplifiable human DNA (especially in diagnostic devices).

On the other hand, a sterilization technique that satisfies all of these requirements does not exist, and so the most appropriate sterilization technology must be chosen to ensure that the device functions properly throughout its shelf life, without causing any unanticipated or detrimental effects on the product's safety or performance. This necessitates the consideration of numerous variables:

- The product's functionality: the comprehension of the product's claim is a critical factor in the consideration of the appropriate sterilization modality for a device, among all the other factors.
- The design attributes: the mechanical properties, microbiological aspects, and biocompatibility of the device after the sterilization process have to be evaluated to determine whether the sterilization procedure can compromise the functionality of the product.
- The configuration: the geometry of the device and the layout of the packaging must be configured to ensure that microorganisms are properly killed when exposed to the sterilizing agent, thereby ensuring the desired sterility assurance levels.

For medical applications, three primary sterilization methods are commonly used: ethylene oxide sterilization, gamma ray sterilization, and electron sterilization, which are discussed in the following sections.

1.2 Ethylene Oxide Sterilization (Chemical Method)

The ethylene oxide (C_2H_4O , usually abbreviated in EO or EtO) is an exceptional sterilizing agent because of its effective bactericidal, sporicidal, and virucidal activity due to its high reactivity and diffusivity [4]. EO reacts with the cellular constituents of organisms, leading to the denaturation of the cell and preventing the ability to reproduce, which makes the impacted microorganisms nonviable [5].

During the EO sterilization process, the medical products are placed inside an airtight chamber where EO gas is insufflated. The gas has to reach all the surfaces that need to be sterilized, penetrating inside the sterile barrier, which is the minimum packaging that prevents the entry of microorganisms and keeps the product aseptic until the time of use. For this reason, EO sterilization can be used only with products with porous packaging. In addition, EO treatment can not be performed on products with liquid inside, since EO is soluble.

Before the sterilization, products are heated and exposed to a controlled humidity level in order to ensure the repeatability of the process independently of the environmental condition to which the products have been ex-

posed before the sterilization process. The EO sterilization process starts with an initial evacuation of the air in the sterilization chamber, since EO vapor is flammable and explosive when mixed with air, as dramatically shown at the Sterigenics sterilization site in Ontario (CA) in 2004, when an explosion occurred inside an ethylene oxide sterilization chamber and an associated thermal oxidizer [6]. Of course, the vacuum rate is chosen to protect package integrity by allowing trapped air inside the package to vent without breaking the seal integrity. As an alternative, nitrogen (which is an inert gas) is injected during the evacuation of air in the chamber when pressure-sensitive products are treated. The EO sterilization is successful only when the right heat, moisture, and gas concentration are delivered for a sufficient amount of time; therefore, before insufflating the EO vapor, steam is injected in the treatment chamber. After the humidification phase, EO gas is injected inside the chamber, with a concentration that guarantees to achieve sterility without reaching a too high level of EO in the product, which might lead to difficulties in the post-sterilization phase, when EO becomes an undesired residual, being a carcinogenic substance. The exposure time, as well as the other parameters, is defined by the process design scientist. Finally, after the exposure time, EO is removed from the chamber, and various washes with nitrogen are performed to reduce product residues. After a safe level of EO residuals, products might be placed out of the sealed chamber, in a heated room, for additional removal of the residual gases.

To validate the EO sterilization process, two methods are typically used: the overkill method, and the combined biologic indicator/bioburden method [4]. The overkill approach uses the biological indicator (BI) to assess the effectiveness of the sterilization process. Figure 1.1 shows an example of a BI, which is a vial that contains a disc with a culture of spores and a nutrient liquid: if spores are still alive after the sterilization process, the liquid changes color and indicates the failure of the process. The population of the BI (typically 10^6 microorganisms of "Bacillus Atrophaeus") and its resistance (i.e. the ability of the microorganisms contained in the BI to survive exposure to EO) have to exceed that of the product population of viable microorganisms, to guarantee that if the sterilization condition is achieved in the BI, it will be achieved also on the product. This conservative approach is likely the most popular due to its simplicity and the robust sterility assurance level that is achieved, despite the fact that it typically results in overestimating process parameters [4, 5].

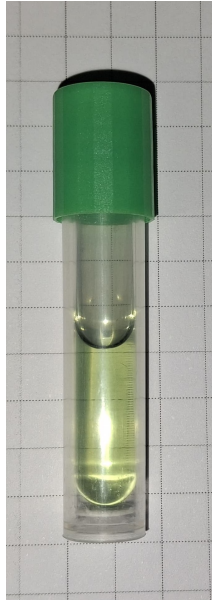


Figure 1.1: Biological indicator consisting of a sealed glass ampoule containing a digest broth and a paper carrier inoculated with *Bacillus Atrophaeus*. When the ampoule is crushed and incubated at the appropriate temperature, the organism can grow. The physical characteristic showing growth is a color change from green to or toward yellow and/or turbidity. No variation in the color means that the sterilization process was successful. Squares in the background are 5 x 5 mm.

The combined biologic indicator/bioburden method is based on the control of the treatment time required to achieve sterilization. This method requires various tests with BI during the sterilization process, and precise knowledge of the product bioburden population, which is (by definition of the ISO 11137) the population of viable microorganisms on or in the product and/or sterile barrier system, which come from various sources of contamination: air, workers, raw materials, machines, environments, and so on. Therefore, the bioburden indicates the quantity and quality (resistance to sterilization) of microorganisms on the product, and a non-controlled bioburden of the product might lead to non-sterile products, although the sterilization process is validated. The bioburden is tested by counting the number of microorganisms, and the average bioburden (on various samples) is expressed in colony forming units (CFU), determined by culturing the sample on an appropriate growth medium and enumerating the viable colonies that develop after incubation under specified conditions. Based on the CFU and on the BI tests, the EO treatment time is therefore assessed.

Typically, an EO treatment for medical products can last from a few hours

to tens of hours, depending on the facility, the product, the treatment plan, and so on. However, multiple pallets of products can be processed simultaneously within the treatment chamber, which typically has a volume of several thousand liters; on average, EtO sterilization corresponds to approximately 3 minutes per box, assuming a standard medical-device box volume of about 50 liters. The main criticality on EO today is related to gas residuals: ethylene oxide (EO) and ethylene chlorohydrin (ECH) residuals are toxic, and so products might require a long aeration phase after the treatment, to reach a residual concentration lower than the limit defined in the ISO 10993-7. In addition, as previously mentioned, products must sustain temperatures up to 60°C, and humidity of also 45%.

Before discussing gamma ray and electron sterilization, it is important to present the key radiation-matter interaction mechanisms relevant to ionizing radiation sterilization; this overview is provided in the following section.

1.3 Radiation-Matter Interaction in Radiation Sterilization

Ionizing radiation, such as electrons and gamma rays, can be used for the sterilization of medical products. By definition of ionizing radiation, in the interaction of the radiation with matter there is a release of energy that is enough to ionize atoms or molecules. More specifically, a microorganism may become nonviable as a result of the interaction with the ionizing radiation, and this is the mechanism at the base of the ionizing radiation sterilization.

The fundamental quantity in the ionization sterilization processes is the dose, which is the energy absorbed from any type of radiation per unit of mass of the absorber [7]. The unit of measure is the Gray (Gy), which corresponds to 1 J/kg.

Acute lethal effects from ionizing radiation in humans are observed at doses exceeding 10 Gy; however, lower doses may also be fatal due to the dose-dependent increase in cancer risk [8]. Such a dose corresponds to a temperature rise of approximately 0.001 °C, indicating that the associated biological effects cannot be attributed to thermal heating. From a biological perspective, the ionization and excitation of atoms and molecules within the cell initiate a complex series of events that could alter the chemical composi-

tion of the biomolecules, potentially leading to cell mutation, transformation, or death.

The part of the cell most sensitive to radiation damage is the DNA, which is a molecule with a diameter of the order of nm (typically 2-3 nm). Following the passage of a charged particle through the cells and the production of ionized and/or excited atoms and molecules, several chemical and physical events occur in rapid succession. Cells are more than 70% water, so most of the absorbed energy gives rise to the formation of radicals $\text{H}\cdot$ and $\cdot\text{OH}$, that are highly reactive molecules. In addition, the DNA can be directly damaged by radiation, which can damage one of the bases of the DNA molecule or can cause a single or double strand breaking of the DNA helix. The extent of the damage depends on factors such as the microorganism's resistance and the surrounding environmental conditions. The dynamic of the interaction also depends on the type of radiation.

X-rays and gamma radiation interact with matter mainly with three possible mechanisms: photoelectric effect, Compton scattering, and pair production. Briefly, in the photoelectric effect a photon (i.e. X-ray or gamma radiation) interacts with electrons around the atoms, kicking out the electron from the atom orbital with a kinetic energy equal to the energy of the photon minus the bonding energy of the electron. In this interaction, the photon is completely absorbed, different from the Compton scattering where the photon transfers only a part of its energy to an electron, which exits from the atom orbital. Finally, in the pair production, the photon interacts with the electric field of the nucleus of the atom, and the photon is converted into an electron and a positron [7]. More details on the three interactions are provided in the following paragraphs, but what comes from this short introduction is that regardless of the initial interaction, photon exposure ultimately leads to the generation of an electron. From that point onward, the interaction mechanism is the same as that of an electron beam. As a result, the effects on a material exposed to electrons, gamma rays, or X-rays are similar. In terms of the fundamental processes responsible for sterilization, these three radiation sources are effectively indistinguishable [9]. The type of radiation is more relevant when considering the spatial distribution of deposited energy within a product or a box of products. Photons penetrate the material and generate electrons at various depths, after which these electrons behave similarly to those in an electron beam. In contrast, electrons from an electron beam begin interacting with the material immediately upon entry. This difference

affects how energy is absorbed and distributed, ultimately influencing the uniformity of the sterilization process.

Radiation-matter interactions are probabilistic, which means that each of the three interaction mechanisms previously mentioned has a certain probability to occur when a photon meets the electron, and that's why photons are gradually converted into electrons as they penetrate the material, rather than all being transformed instantly upon initial contact. The interaction probability strongly depends on the energy of the photons: for low-energy photons, the photoelectric effect is dominant, while for about 1 MeV photons, like the ones emitted by a Co-60 source, the main mechanism is the Compton scattering. In general, the interaction probability increases as the energy decreases, and for the photoelectric effect, the probability goes as $Z^n/E^{3.5}$, where Z is the atomic number and n is in between 4 and 5, while for the Compton effect, the relation is Z/E [7]. The probability of interaction is expressed by the attenuation coefficient μ , which quantifies the decrease in the intensity of a narrow beam of monoenergetic photons:

$$I = I_0 e^{-\mu x}$$

where I is the intensity of the beam penetrating a layer of material with thickness x , with initial intensity I_0 . Considering 1 MeV photons, the attenuation coefficient amounts to 0.07072 cm^{-1} (according to NIST tables [10]), and so the intensity of the beam crossing 5 cm of water is decreased of about 30%, while 10 MeV electrons are almost completely stopped in 5 cm of water.

The interaction of energetic electrons ($> 100 \text{ eV}$) with matter is described by the Bethe–Bloch equation, which describes the average energy loss per unit path length—known as the stopping power (S). This energy loss arises from ionization and excitation of atoms in the material, commonly referred to as collisional losses due to Coulomb interactions. As a first approximation, the stopping power for electrons is proportional to [7]:

$$S = -\frac{dE}{dx} \propto \rho \frac{Z}{A} \frac{1}{E}$$

The linear energy transfer is proportional to the density ρ , to the ratio of the atomic number Z and to the atomic mass number A (which is almost constant for light materials, about 0.5) and inversely proportional to the energy. In principle, the stopping power of a material allows for an estimation of the

average distance an electron travels within it. However, this distance differs from the actual penetration depth, as an electron's trajectory is not linear due to multiple scattering events that continuously alter its direction. As a result, energy deposition does not occur uniformly along a straight path but instead builds up at a distance approximately equal to half of the electron's penetration depth [9].

Other than losing energy through Coulomb interactions, electrons also emit photons through the Bremsstrahlung process: more precisely, X-rays are emitted when electrons are accelerated (or decelerated), and the intensity is proportional to the acceleration of the electron. Therefore, Bremsstrahlung is more important for high Z materials, for which the electric field of the nucleus is stronger, and so the acceleration; for this reason, targets of tantalum ($Z = 73$) or tungsten ($Z = 74$) are typically used for X-ray conversion of electron beam in X-ray sterilization facilities. The energy spectrum of emitted X-rays depends on the energy of the electrons and goes up to the maximum energy of the electrons, with peaks at the characteristic energies of the material (i.e. the energy of photons emitted from the de-excitation of atoms excited by the ionizing radiation).

The depth-dose curves shown in Figure 1.2 represent the dose deposited in function of the depth for electrons and photons. Also for photons, a build-up effect is visible, due to the fact that energetic electrons generated in the first layers of the material deposit their energy more in depth in the material. After the build-up region, the expected decrease is observed.

It is straightforward that electrons are much less penetrating than gamma (and X-ray) radiation, and for this reason, electron sterilization is typically performed on a single box (about 50 liters of volume), while gamma and X-ray sterilization is performed on the entire pallet (about 3'000 liters of volume).

In a homogeneous material, the dose uniformity ratio (DUR), which is the ratio between maximum and minimum dose (further details in Chapter 1.4), can be easily assessed from the depth-dose curve. The DUR for electron irradiation can be improved by increasing the energy of the electron beam, but the threshold of 10 MeV must not be exceeded; otherwise, the induced radioactivity in products shall be assessed according to ISO 11137. A good practice to reduce the DUR is to perform a two-sided irradiation; the resulting depth-dose curves are shown in Figure 1.3, where two depth-dose curves are shown for 9.5 cm and 7.5 cm thick targets of water.

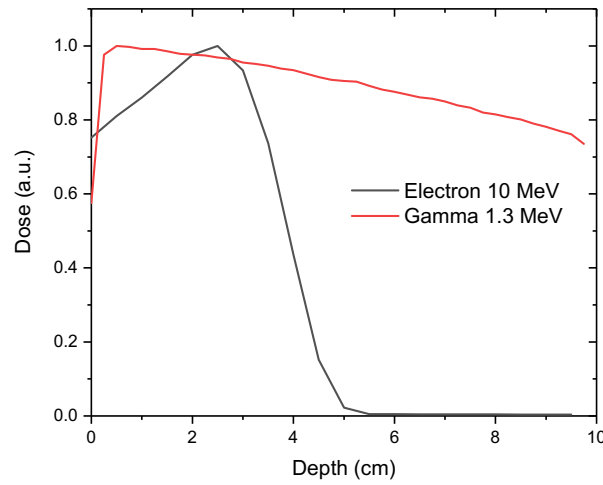
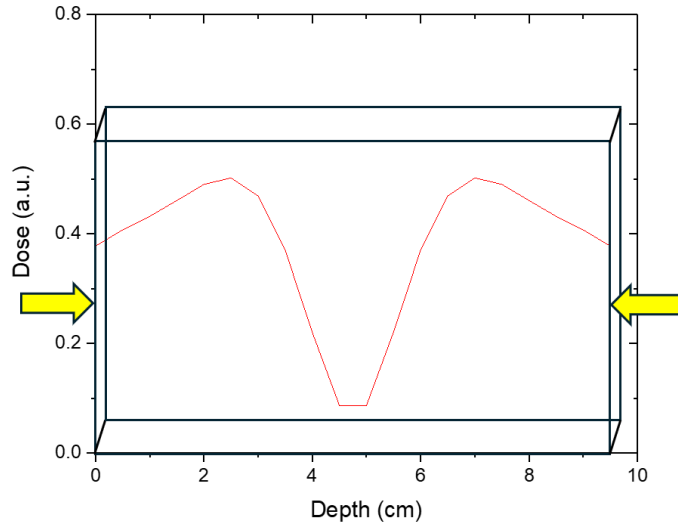


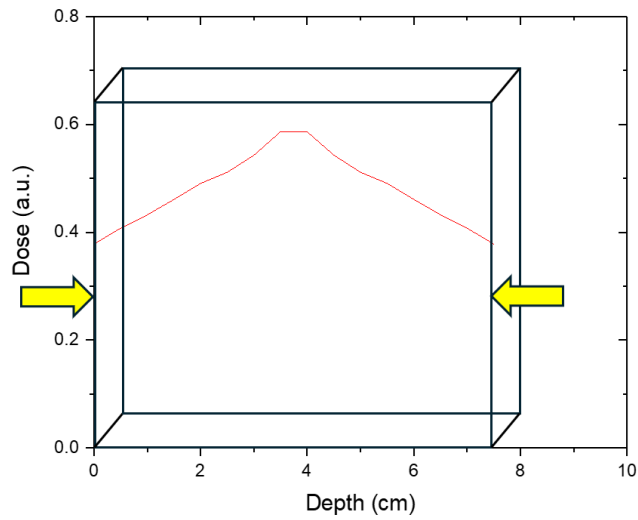
Figure 1.2: Dose depth curve for electrons at 10 MeV and gamma at 1.3 MeV in a slab of water (1 g/cm^3 density) 10 cm thick, as obtained from Geant4 simulations.

The typical "apparent" density (i.e. the mass of the box over its volume) of plastic medical products ranges between 0.1 and 0.5 g/cm^3 , but depth-dose curves for electrons linearly scale with the density. In fact, the stopping power is linear with density, and so what matters is the product of depth and density, which is expressed in g/cm^2 . Since depth-dose curves reported in Figures 1.2 and 1.3 are calculated for water with a density of 1 g/cm^3 , the same curves hold for the standardized depth expressed in g/cm^2 : therefore, the penetration depth of almost 5 cm of 10 MeV electrons in water can also be expressed in terms of 5 g/cm^2 . As a rule of thumb, for a box of products the maximum penetration is given by the ratio of the standardized penetration depth (5 g/cm^2) over the average density; for example, 10 MeV can penetrate a box of products of density 0.2 g/cm^3 for $5 / 0.2 = 25 \text{ cm}$.

Of course, products are not made of water, but the stopping power depends on the ratio of Z/A , and so plastic, which is composed of light elements, can be approximated to water. Nevertheless, it is possible to convert a dose in water into a dose in another material according to Bragg-Gray theory, which states that by having a material g with a small portion of another material m inside and knowing the dose in the surrounding material D_g , it is possible to estimate the dose in the other material D_m according to the formula:



(a)



(b)

Figure 1.3: Dose depth curve for electrons at 10 MeV in a 9.5 cm (a) and 7.5 cm (b) thick target of water, with double irradiation (as indicated by the yellow arrows), as obtained from Geant4 simulations.

$$D_m = D_g \frac{S_m/\rho_m}{S_g/\rho_g}$$

This relation comes from the definition of dose, which can be expressed as:

$$D = \int \Phi_E \frac{S}{\rho} dE$$

where Φ_E is the differential energy distribution of the electron fluence, S is the stopping power and ρ is the density of the material. In case of a monochromatic fluence of electrons, the relation simplifies to:

$$D = \Phi \frac{S}{\rho}$$

from which can be easily obtained the relation that allows to estimate D_m from D_g , assuming that the fluence in the two materials is the same (that's why the Bragg-Gray theory's main hypothesis is of having a material g with a small portion of another material m inside). In addition, this relation underlines that the dose does not directly depend on the density; in fact, the S/ρ coefficient only depends on A , Z (and on the ionizing potential of the material). On the other hand, the fluence of electrons in a material depends on the density, and so inhomogeneities in density should be taken into account, for example, in simulations to evaluate the dose in a box of product. Finally, Figure 1.4 reports the S_m/ρ_m in function of energy for different materials normalized to the S_w/ρ_w of water, i.e. $(S_m/\rho_m)/(S_w/\rho_w)$ and so D_m/D_w : as expected, the ratio is almost one for most of light materials, especially at higher energies. This result will be significant for dose map simulations discussed in Chapter 2, where virtual dosimeters are defined of air to minimize their impact on the electron fluence within the box, assuming that the dose in air equals the dose in water, which is the reference material for dosimetry systems.

As a final remark, although direct electronuclear reactions are in principle possible, their probability is extremely low; consequently, electrons do not directly induce radioactivity in materials under practical conditions. Nevertheless, by the production of Bremsstrahlung X-rays, they can induce radioactivity primarily via three mechanisms:

- A photon interacts with a nucleus, knocking out a neutron, and the residual nucleus becomes unstable and decays, emitting radiation. This nuclear reaction is called (γ, n) reaction.

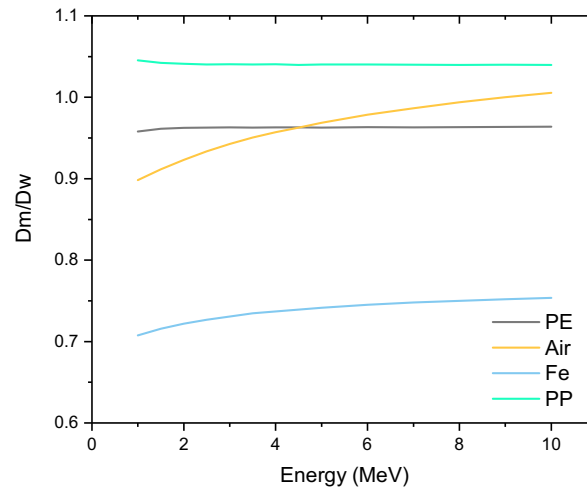


Figure 1.4: Ratio of dose in the material with respect to the dose in water for different materials, according to Bragg-Gray theory for electrons (stopping power in function of the energy from the NIST database[10]).

- The neutron generated in the above interaction can interact with another nucleus, and the target nucleus becomes radioactive.
- Photons or neutrons can excite a nucleus, which becomes radioactive.

However, the probability of these interactions strongly depends on the energy of the photons, and ISO 11137 imposes a limit of 10 MeV on electron beam energy and 7 MeV on X-rays to avoid induced radioactivity into the material. In fact, the cross section of (γ, n) reactions for iron and copper, as an example, for photons at 10 MeV is in practice zero, as shown in Figure 1.5.

1.4 Ionizing Radiation Sterilization (Overview)

In the ionizing radiation sterilization techniques, medical products are exposed to a field of ionizing radiation, such as electrons and gamma rays, which release energy to the contaminating microorganisms. To achieve sterilization, it is necessary to deliver a minimum dose higher than the sterilizing dose, which is assessed through two possible methods, according to the ISO 11137-2:

- Bioburden Method: The sterilizing dose is established on the base of

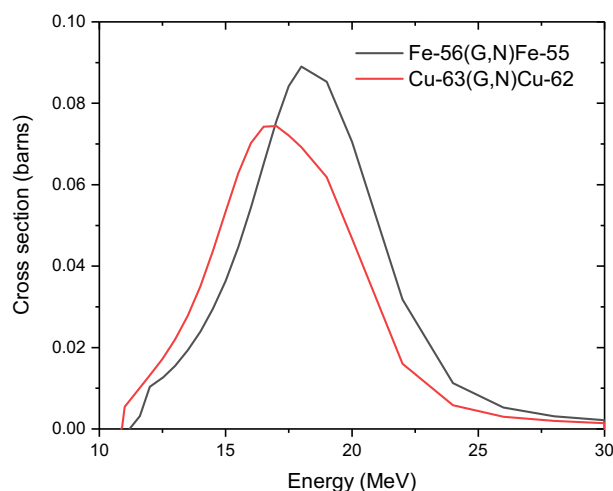


Figure 1.5: Cross section of the (γ, n) reactions for iron and copper, from the TENDL database [11].

the population of viable microorganisms on the product (or a representative product of a family of products) and/or sterile barrier system.

- VDMax Method: 25 kGy is used as the sterilizing dose for any product. This approach is more conservative than the first one, but simpler.

The dose delivered to each product within a box is not uniform due to factors such as radiation beam attenuation, beam scattering, and edge effects, which are discussed in more detail in Chapter 2. Ideally, the minimum dose required for sterilization would be evenly distributed throughout the box. However, dose non-uniformities result in certain points receiving significantly higher doses. In irradiation sterilization, the maximum dose is also a critical factor, as higher doses can cause damage to the products. Therefore, tests should be conducted to verify the functionality of products exposed to the maximum dose.

The dose uniformity ratio (DUR) is typically used to express the dose uniformity of the treatment, and it is defined by the ratio of the maximum to the minimum absorbed dose within the irradiation container (ISO 11137-3). Of course, the DUR is not a stable metric, since it depends on the ratio of only two values of doses, while, for example, the variance of the doses depends on the entire population of dose values, but it still provides immediate information on the uniformity. The DUR depends on the product, on the packaging, and on the sterilization setup, as discussed in Chapter 2. In

addition, the DUR strongly depends on the sterilization process: the electron sterilization typically has a higher DUR than the gamma sterilization, although electron sterilization deals with single boxes of products at a time, while gamma sterilization with entire pallets. On the other hand, the dose rate offered by the electron sterilization process is about 2-50 kGy/s, which is much higher than the 1-10 kGy/h in a gamma sterilization facility. In the end, the electron sterilization is the fastest one, with about 2 min/box, while gamma sterilization takes about double the time.

From a regulatory perspective, all radiation sterilization techniques are considered equivalent, and it is not required to specify whether a product was treated with electrons or gamma radiation. According to the ISO 15223, the label of an irradiated product should simply display the symbol "R", indicating radiation treatment, to differentiate it from "EO" the one that denotes ethylene oxide sterilization (as an example). However, electron and gamma sterilization differ significantly in terms of operation. Therefore, the following sections present the gamma, electron, and X-ray sterilization techniques individually from an operational perspective.

1.4.1 Gamma Sterilization

Inside a gamma ray sterilization facility, boxes of products are placed in trays that move through a vault where the gamma source is exposed. The gamma source typically consists of an array of Cobalt-60 bars, which emit photons with energies of 1.17 and 1.33 MeV (gamma rays). Some facilities, however, use Cesium-137 as the gamma source, which emits gamma rays at 0.662 MeV. Within the vault, the trays follow a designated path, passing alternately in front of and behind the source to ensure a uniform dose distribution across the products. The number of gamma ray emissions per second in these facilities is impressive: about 1 MCi (mega-Curie) of activity, which is 10^{16} disintegrations per second (Bq/s). Of course, such an intense radiation field has to be contained inside a vault, with meter-thick walls of concrete. The benefits of using gamma rays for sterilization of medical products are multiple: the packaging has not to be porous as for EO sterilization, and products are not exposed to high levels of temperature and humidity. In addition, no toxic residuals are left in the product after the treatment. However, some materials are not compatible with radiation sterilization, as discussed in Chapter 3, which suffer from embrittlement, change of color/odor, and viscosity in liquids, due to radiation. Finally, Cobalt-60 sources continuously emit radiation,

posing ongoing safety concerns. Moreover, their activity gradually decreases over time; thus, the bars must be reloaded annually, as the half-life of Co-60 — the period over which its activity is reduced by half — is approximately five years.

1.4.2 Electron Sterilization

The core of an electron sterilization facility is the radiation source, which is a particle accelerator. This machine is needed to accelerate electrons, usually at 10 MeV. Boxes of products to be treated are loaded on a conveyor, which moves the boxes inside the vault, where boxes pass through a "curtain" of high-energy electrons produced by the accelerator. The most common accelerating machine is the so-called LINAC, which stands for LINear ACcelerator. A LINAC can produce a 10 MeV electron beam by progressively accelerating electrons using variable electric fields. An alternative to the very common design of the LINAC is offered by the Rhodotron, which is described in the details at the beginning of Chapter 2. An important advantage of electron sterilization (and X-ray sterilization, described in the following Section) is that ionizing radiation is produced using a machine, which can be turned off and stops emitting radiation, in contrast to gamma sources. In any case, during operations the radiation should be confined, and so the particle accelerator and the treatment room are surrounded by meter-thick walls of concrete.

With respect to gamma rays, 10 MeV electrons can penetrate a smaller distance inside the product. The penetration depth would increase by increasing the energy of electrons, but 10 MeV is the limit over which the potential for induced radioactivity in products shall be assessed according to ISO 11137 (the analogous limit on the X-rays is 7 MeV). However, as previously discussed, medical products are packaged in boxes with an average density of about 0.20 g/cm^3 , and so 10 MeV electrons can penetrate about 25 cm of products, which is the typical height of a single box of products. Therefore, electron sterilization is typically irradiating one single box under the beam at a time, while in a gamma sterilization facility, the irradiation is performed on pallets of boxes inside the treatment room. Apart from this, electron sterilization has the same advantages and disadvantages of gamma sterilization (such as absence of residuals and potential product damage), but it results in a faster process, as previously reported.

1.4.3 X-ray Sterilization

The electron accelerator is also the core of X-ray sterilization facilities: in fact, impinging the electron beam on a proper high atomic number target, as tantalum or tungsten, leads to the emission of X-rays through Bremsstrahlung, which are ionizing radiations (high energy photons) used for sterilization. The broad energy spectrum of photons emitted in the Bremsstrahlung process goes up to the energy of the electron beam (5 MeV typically), although most of the fluence is at lower energy. For this reason, X-ray sterilization combines the penetration capabilities of gamma sterilization, with the advantage of having a radiation source that can be turned off, as in an electron sterilization facility.

The X-ray sterilization process starts with the loading of pallets of products on trays, which move the products inside the vault where they pass in front of the exit window of the X-ray source. Trays move and rotate in front of the exit window to guarantee that the deposited dose is uniform in products.

Unfortunately, the Bremsstrahlung conversion is about 3% - 7% in terms of power to the electron beam to power the X-rays. The conversion of beam power to dose for electrons and X-rays is comparable [12], therefore, X-ray sterilization results in being much less efficient compared to electron sterilization in terms of costs of operations.

To summarize, ionizing radiation can be successfully used for sterilization, especially for treating all the devices that contain liquids or gels and/or have impermeable packaging, which therefore cannot be treated using ethylene oxide. Compared to EO, radiation techniques might be more efficient in terms of treatment time, but radiation may induce damage to the products because of the direct interaction of radiation with the products, but also because of the temperature during irradiation, which can reach 60°C in electron sterilization. Electrons are less penetrating than gamma/X-rays, and so the treatment is performed on single boxes of products rather than entire pallets treated in the gamma facilities. As a final remark, radiation sterilization is not capable of reducing human DNA, and so devices used in forensic science cannot be sterilized using radiation to obtain a DNA-free product. The above considerations are summarized in Table 1.1.

Radiation sterilization relies on accurate dose assessment and measurement to ensure effective treatment. This process is carried out using dosimeters, which come in various types, each with specific properties suited for

Device characteristics	EO	Gamma/X-ray	Electron
The device materials are temperature sensitive	Yes	To be evaluated	To be evaluated
The device materials, or its packaging configuration, have high density	Yes	Yes	To be evaluated
The device contains liquids or gel	No	Yes	To be evaluated
Some parts of the device are soaked in aqueous solution	No	Yes	Yes
The device is vacuum packed	No	Yes	Yes
The geometry of the device does not allow gas penetration and exit (tunnels, long and narrow tubes, etc.)	No	Yes	Yes
The device (or its packaging) is sensitive to pressure changes	No	Yes	Yes
The packaging of the device is waterproof	No	Yes	Yes
The packaging of the device is not porous	No	Yes	Yes
The device requires hDNA reduction	Yes	No	No

Table 1.1: Applicability of sterilization methods based on device characteristics.

different applications, and the most common dosimeters used in radiation sterilization are presented in the next Section.

1.5 Dosimetry in Radiation Sterilization

In the field of radiation sterilization, the requirements for dosimeters are good precision on the measured dose in the range of 1 - 100 kGy, compact size, and stability under varying environmental conditions and over time. Passive detectors are particularly well-suited to these demands, offering reliable and consistent performance. This Section provides an overview of the most commonly used passive dosimeters in industrial sterilization, highlighting their characteristics, advantages, and applications.

1.5.1 Alanine Dosimeters

The alanine dosimeters are pellets containing alanine ($\text{CH}_3\text{CH}(\text{NH}_2)\text{COOH}$), which is an amino acid composed of a carboxylic group (COOH), amino group (NH_2), a methyl (CH_3) and a hydrogen atom, all bound to a central carbon atom. The interaction of ionizing radiation with alanine results in the formation of radicals, which are molecules or ions with unpaired electrons that give

paramagnetic properties to the material [13]. By analyzing the irradiated alanine with an Electron Paramagnetic Resonance analysis (EPR), it is possible to measure the EPR spectrum, whose intensity is related to the number of paramagnetic centers created by the ionizing radiation, and so to the dose.

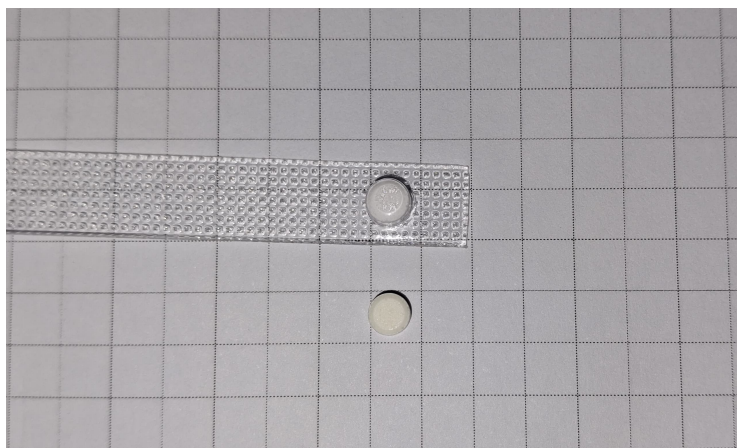


Figure 1.6: Alanine pellets: in a blister (top) and not packaged (bottom). Squares in the background are 5 x 5 mm.

Alanine dosimeters are suited for a large range of doses, from 1 Gy to 150 kGy, that covers the typical sterilization dose range, and they are available as small cylindrical pellets of 4 mm diameter and 2 mm height, as shown in Figure 1.6. As previously mentioned, the readout of the dosimeter is performed using an EPR spectrometer, and from the EPR spectrum it is possible to determine the absorbed dose by the alanine through the dosimetry system calibration, which depends on the type of radiation (gamma, electrons, energy of the radiation, etc.), dose rate, irradiation temperature, humidity, and time after irradiation. In particular, temperature has a significant impact on the dose reading, and a correction factor of about $+0.10\%/^{\circ}\text{C}$ should be applied [14]. Of course, the temperature in the box during irradiation must be measured, typically using thermolabels. On the other hand, alanine dosimeters are characterized by short time stability [15], and the response is not significantly affected by humidity and dose rate in operative conditions [16].

The advantage of using alanine with respect to other commercial dosimeters is mainly the small measurement uncertainty that can be achieved, from 2% (reference standard) to 4% (routine monitoring) at a 95% confidence level. On the other hand, the EPR spectrometer is quite an expensive instrument, and also the alanine pellet itself is more expensive than other commercial dosimeters.

1.5.2 Radiochromic Dosimeters and CTA Strips

The interaction of ionizing radiation with radiochromic films (RCFs) induces various processes in the sensitive element, which manifest as a color change at the macroscopic level that is proportional to the absorbed dose [17]. The change in the optical properties is measured using a spectrophotometer, which determines the post-irradiated absorbance or the amount of color change induced by the irradiation. Radiochromic films are typically very thin 10 mm x 10 mm films, and the dose range goes from about 100 Gy to more than 150 kGy. The measurement uncertainty with RCF is typically higher compared to alanine, and amounts to approximately 6% at a 95% confidence level. In addition, RCF typically are affected by short-term instability, i.e. the measured absorbance grows with time; to accelerate the stabilization, it is sometimes recommended to perform a heat treatment of the film after the completion of the irradiation, which takes from a few minutes to half an hour. Temperature is also a limit during irradiation: in fact, some RCF cannot be used at irradiation temperatures higher than 60°C, which are not unusual with electron irradiation [18].



Figure 1.7: RCF films (on the left) and radiochromic PMMA dosimeters (on the right). Squares in the background are 5 x 5 mm.

Small PMMA parallelepipeds of dimensions 30 x 11 x 5 mm containing a radiochromic dye are also a widely used type of dosimeter. The reproducibility of the measure for PMMA dosimeters amounts to 6% at a 95% confidence level [19]. In addition, PMMA dosimeters are quite stable only for temperatures below 40°C, but they are characterized by short-term post-irradiation stability [20]. Due to the temperature constraints, PMMA dosimeters are more used for gamma/X-ray sterilization than for electron sterilization.

Finally, cellulose triacetate (CTA) strips are other dosimeters also based

on the alteration of the optical properties of the sensible material. CTA dosimeters are film dosimeters whose optical density increases by radiation exposure, and can be used in a wide range of doses, from 10 kGy to 300 kGy [21]. The reading of the film is performed in the UV spectrum, and it is possible to read continuously long strips of film; this might be useful for dose mapping, but also to measure, for example, the uniformity of the electron beam along the scanning direction.

The Electron Sterilization Process in Copan

Copan (Via F. Perotti 10, Brescia - Italy) is an Italian company that develops products for the collection of biological samples used in the diagnosis of infectious diseases, human genomics, environmental, and forensic applications, as well as automated laboratory solutions. Copan is based in Brescia, but it has productive plants and offices in the USA (California and Puerto Rico), Japan, China, Australia, and in the next future also in Vietnam. During COVID-19, Copan produced more than two billion swabs, a volume enough to be able to test, at least once, more than a quarter of the world's population[22].

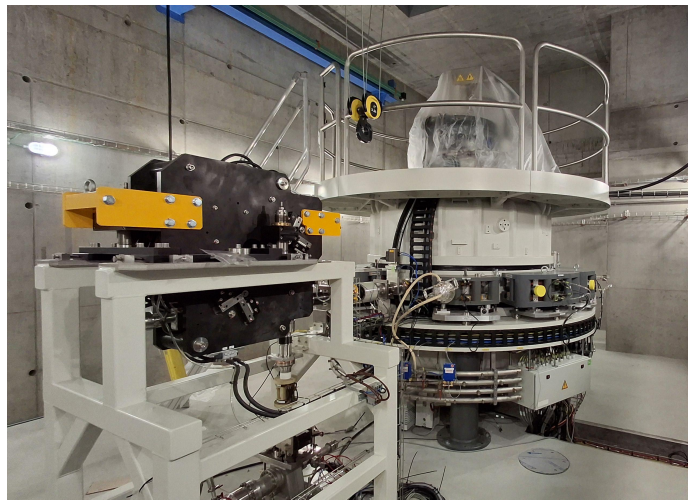
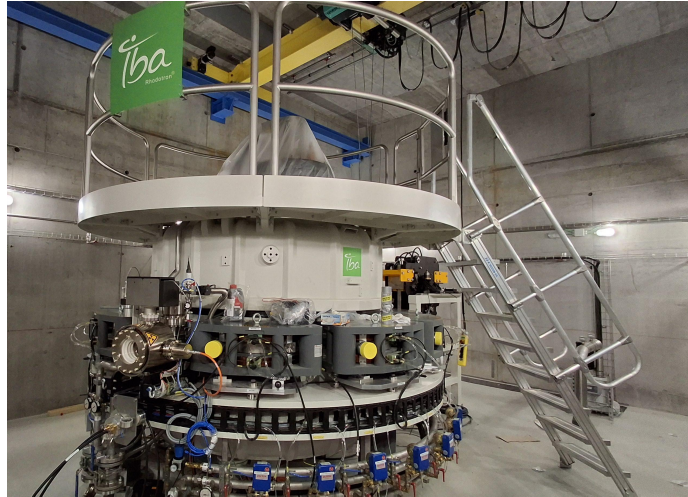
The CHAoS project, related to the installation of Copan in-house Accelerator for Sterilization, was launched in 2022. In 2025, the project advanced to the construction phase with the establishment of a new sterilization facility. The new plant is built in Brescia, and hosts a Rhodotron, an electron accelerator produced by IBA that is widely used for industrial applications, which is described in more detail in Section 2.1. The internalization of the process will lead to an increase in the efficiency of the production process (reduction of time-to-market) and to a reduction of the environmental impact (reduction of road transport, for sterilization by third parties). The following sections present a detailed description of the sterilization plant and process, including an in-depth analysis using Monte Carlo simulations. These simulations offer further insight into the dose distribution within a representative Copan product and serve as a foundation for evaluating and optimizing the sterilization setup.

2.1 Rhodotron Accelerator

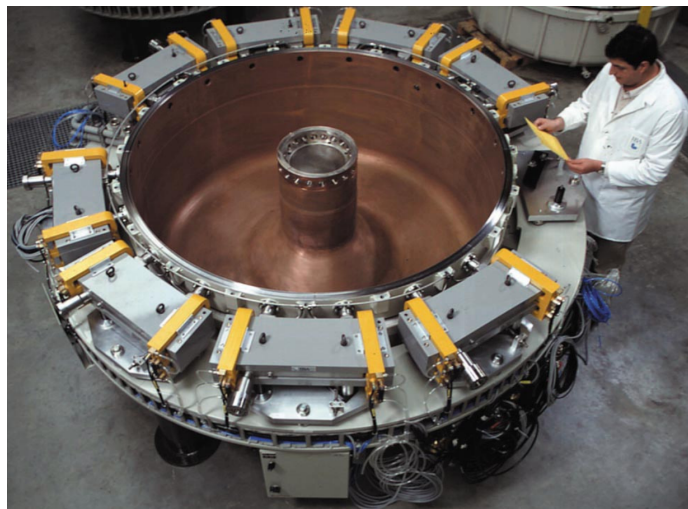
The core of the sterilization plant is the electron accelerator, which, in the case of Copan plant, is a Rhodotron machine produced by IBA (3, Chemin du Cyclotron, Louvain-La-Neuve - Belgium). The Rhodotron, invented by J. Pottier in 1989 [23], is an electron accelerator widely used today in the medical, food, and polymer industries because of its compactness, reliability, and economy [24]. This machine, shown in Figure 2.1 consists of a toroidal resonant cavity that accelerates electrons with an RF field: the electrons gain from 0.8 to 1.2 MeV of energy per pass through the cavity, and by multiple passes it is possible to reach energies up to 10 MeV [25], that is, the energy limit over which, according to ISO 11137-1, the potential for induced radioactivity in irradiated products shall be assessed, since γ - n reactions could potentially activate the products [26].

The trajectory of electrons in the cavity is shown in Figure 2.2, and gives rise to the name of Rhodotron: "rhodos" in Greek means rose [26]. In a few words, the electron gun emits electrons along the diameter of the cavity, and the electric field accelerates the beam until it exits the cavity. Bending the electron beam and reinjecting it into the cavity allows successive accelerations along diametrical trajectories. Such bending is performed with the bending magnet, that deflects the beam of 198° and sends it back toward the cavity. Meanwhile, the electric field inside the cavity reverses polarity, and the re-injected beam from the magnet is further accelerated. The same inversion of polarity happens when electrons pass through holes in the hollow inner conduct, so that the beam is continuously accelerated in the cavity. With 9 deflection magnets and 10 passes, the final electron energy is 10 MeV [27].

More in the details, the toroidal cavity of the resonator can be simplified as a $\lambda/2$ coaxial line short-circuited at both ends, as shown in Figure 2.3. The first Rhodotron was designed to resonate at a frequency of 107.5 MHz, and this frequency is still in use in modern Rhodotrons, because it is possible to use a tetrode tube for the RF power amplifier, which is more efficient and less expensive than the klystrons needed for higher frequencies [27]. However, certain models of Rhodotron have been designed to resonate at double the frequency [26], which offers the possibility of halving the height of the cavity, since the frequency of the mode inside the cavity only depends on the cavity height, but also the downside of an increase in the skin effect resistivity, which for copper depends on the square root of the frequency [23].



(a)



(b)

Figure 2.1: a) Rhodotron TT300 during the installation at Copan sterilization plant, b) Internal view of the accelerating cavity [25], made out of welded plates of steel plated with a copper layer.

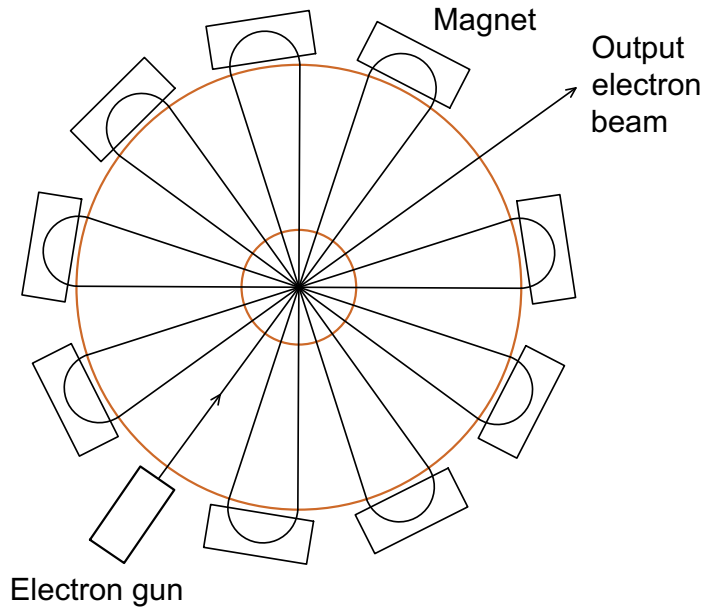


Figure 2.2: The trajectory of the electron beam as seen from the planar view of the cavity of the Rhodotron.

The electric and magnetic fields inside the cavity are described by the following equations (λ is the wavelength of the RF, and z is the axial coordinate):

$$E = \frac{E_0}{r} \cos \frac{2\pi z}{\lambda} \sin(\omega t + \phi)$$

$$B = \frac{B_0}{r} \sin \frac{2\pi z}{\lambda} \cos(\omega t + \phi)$$

Notably, in the median plane of such a resonator, the electric field is radial, and the magnetic field is zero; therefore, electrons accelerated within this plane are not subjected to parasitic deflection [23].

The oscillating electromagnetic field inside the cavity is self-consistent with the electric current that flows on the surface of the cavity, which causes heating of the cavity and power loss. This power loss is proportional to the square of the voltage inside the cavity, and amounts to less than 100 kW in modern Rhodotrons [27]. The other important contribution to the total power loss in the cavity is, of course, due to the acceleration of the beam, which is proportional to the cavity voltage and the beam current [28].

With respect to a conventional LINAC, the interior wall surface area of the Rhodotron is several orders of magnitude larger, and so heating is less se-

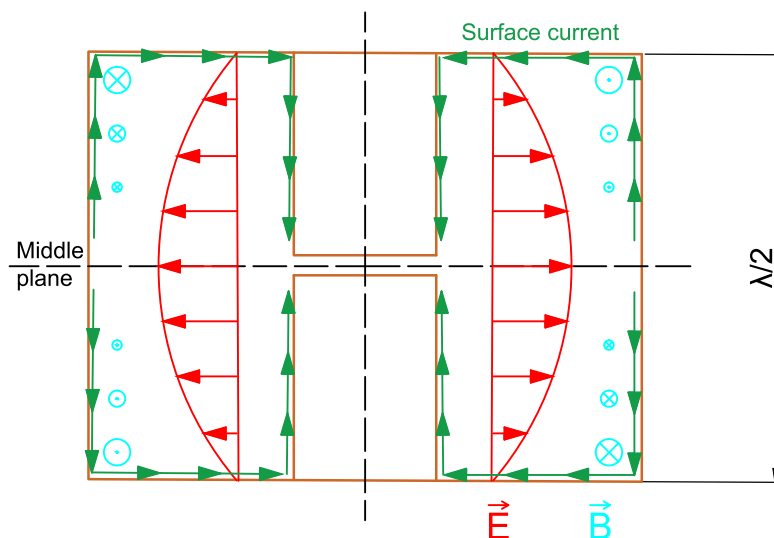


Figure 2.3: $\vec{E}$ and $\vec{B}$ inside the cavity, as seen from an axial section.

vere. The cooling system is divided into two circuits (primary and secondary), which operate with ordinary water.

All the beamline and the cavity are, of course, under vacuum conditions to avoid electrons scattering with air particles, destroying the beam.

The electron source (shown in Figure 2.4), located outside the cavity, is in phase with the RF, and injects electrons when the field is accelerating. The phasing of the electron gun is crucial to avoid that electrons entering the cavity with the wrong phase are lost in the first accelerating step, producing excessive heating in the chamber [24]. At the injection, electrons have an energy of few tens of keV, and this limits the beam current in the cavity because of charge effects in the injection area [24]. After the initial acceleration phase within the cavity, the electrons rapidly approach the speed of light [26]. The inner and outer radii of the toroidal conductor have been carefully designed to maintain synchronization between the electron beam and the electric field within the cavity, ensuring continuous acceleration [28].

The focusing of the beam is mainly achieved by the deflecting magnets shown in Figure 2.5: the horizontal (transverse) focusing is due to variations in the electron trajectories within the dipole magnets, and vertical focusing is obtained with edge focusing [24, 25]. In addition, the electric field distribution at the cavity beam holes also provides a focusing of the beam [29].

Finally, phase focusing also occurs within the dipole because higher energy electrons will travel a longer path in the magnet, and the energy gain in

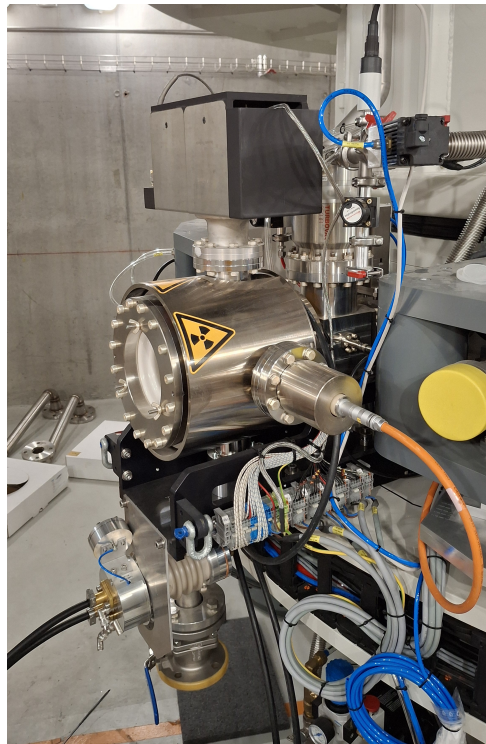


Figure 2.4: Rhodotron electron source during the installation at Copan sterilization plant.



Figure 2.5: Rhodotron bending magnet (one out of nine) during the installation at Copan sterilization plant.

the next acceleration will be smaller [25].

When the beam exits the cavity, with an energy of 10 MeV, it is bent at 270° towards the floor by a bending magnet as the one shown in Figure 2.6, where there is an aperture that allows the beam to reach the conveyor that is downstairs with respect to the Rhodotron.

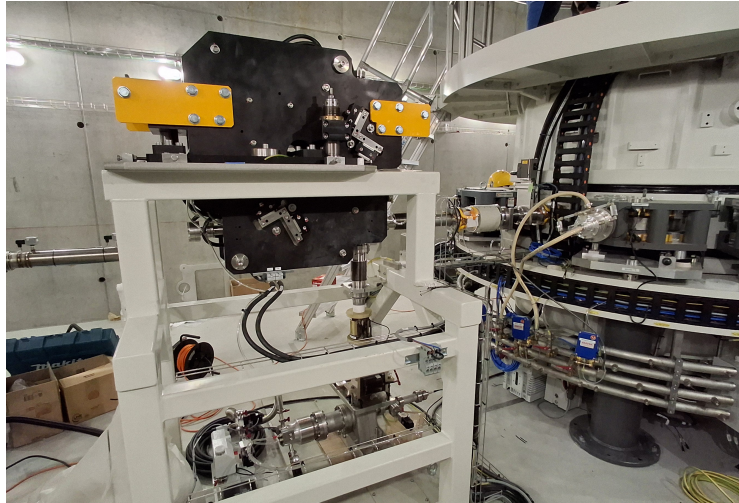


Figure 2.6: Rhodotron 270° bending magnet during the installation at Copan sterilization plant.

The beam is focused thanks to quadrupoles and magnetic lenses (beam-line is partially shown in Figure 2.7), and it is then scanned in a direction perpendicular to the direction of motion of boxes on the conveyor, with a typical frequency of 50 Hz.

This scan generates a uniform surface dose distribution in the box of products under irradiation, and the high-frequency scan avoids "zig-zag" dose patterns in the products. After the scanning magnet, there is a second bending magnet assembly (called pseudo-parallel magnet) that reorients the electrons, so that the resultant beam is non-divergent, in order to obtain a "curtain" of electrons perpendicular to the conveyor, for increased dose uniformity and less beam power wastage in the fall-off zones. In addition, the scan width and its offset with respect to the center of the conveyor can be adjusted to match the dimensions of boxes under treatment. Finally, the exit window of the beam is a sheet of titanium a few tens of μm thick. The scan horn and part of the conveyor inside the bunker are shown in Figure 2.8. However, this is not the only configuration, and certain models of Rhodotron are configured to generate X-ray radiation through Bremsstrahlung, impinging the beam on a heavy target of tungsten.

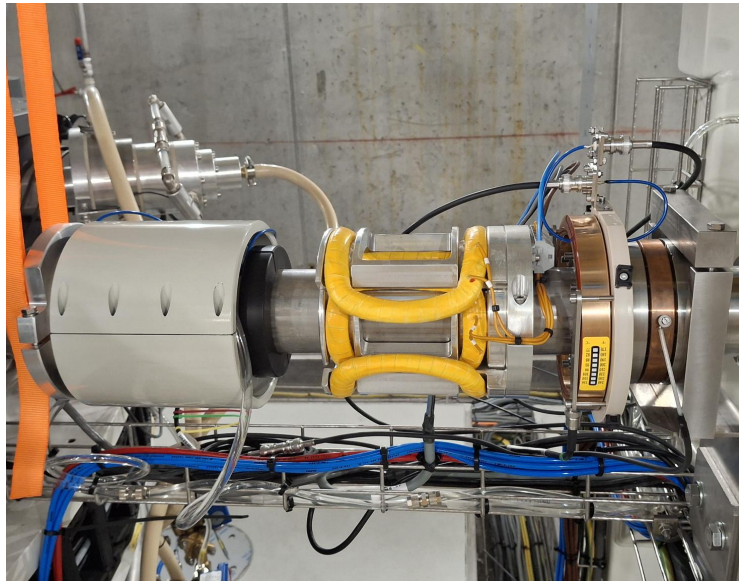


Figure 2.7: Rhodotron exit beamline during the installation at Copan sterilization plant.

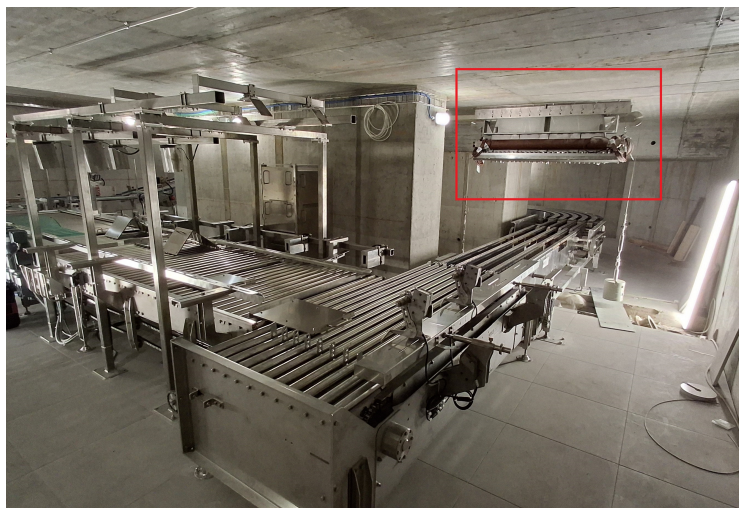


Figure 2.8: Rhodotron scan horn (highlighted by the red rectangle) and conveyor system during installation at the Copan sterilization plant.

2.2 Copan Sterilization Plant

The Rhodotron that will be installed at the Copan site is a TT300 machine, with maximum beam power at 10 MeV of 300 kW, operating in pulse mode. Pulsing the beam allows delivering the same average current, but reducing the time in which the RF system is switched on, saving electric energy and improving the efficiency of the machine.

Naturally, the efficiency of the machine improves with increasing beam power, as constant power losses—such as RF power—become less significant in comparison. Therefore, it is advantageous to operate the Rhodotron at maximum power, corresponding to an average pulsed-mode current of 5 mA. Maximum power also allows obtaining the same dose in less exposure time, and so running the Rhodotron at full power improves the efficiency of the plant also from the operative point of view.

The overall dimension of the machine is 3.0 m in diameter and 2.4 m in height, for a total weight of 11 tons. The machine is installed inside a bunker made of at least 1 m thick concrete walls. At the level of the Rhodotron (first floor of the building), there is the supply room, and the water cooling room; one level below (ground floor), there is the treatment room and the control room. Boxes of products to be treated are placed on a conveyor (realized by OCME, an Italian company specialized in the design of conveyors for the sterilization industry), that transports the boxes from the storage room to the treatment room.

Each product (or family of products) has its own sterilization recipe, which includes all the sterilization plant parameters that ensure the products receive the minimum dose required for sterilization. Furthermore, the irradiation should achieve a homogeneous dose distribution throughout the product box while using the minimum amount of energy and time. Inside the sterilization recipe, the following parameters are defined:

- Average beam current.
- Speed of the conveyor under the beam.
- Number of passages under the beam.
- Scanning width and offset.

The definition of the recipe is therefore at the base of the optimization process of the sterilization plant, and it is performed during the Product Qualification phase (PQ), through an experimental dose mapping of the product.

In this phase, Monte Carlo simulations are very helpful in guiding the placement of the dosimeters. In fact, using Monte Carlo simulations, it is possible to estimate the distribution of dose inside the box of products—the dose map—and so to assess the position of the minimum and maximum dose. Furthermore, the simulated dose map can be used to estimate the sterilization recipe parameters, but simulations can also be used at a higher level in the design of the product, to optimize, for example, the packaging, materials, and so on. In the next section, various studies with Monte Carlo simulations on a representative Copan product are reported, and some strategies to optimize the dose distribution and the sterilization process are evaluated.

2.3 Dose Map Simulations Using Geant4

Monte Carlo codes are extensively employed across a range of physics disciplines. In particular, Geant4 [30] is a Monte Carlo simulation toolkit designed for modeling the interaction of particles with matter. It is widely applied in areas such as high-energy physics [31], medical physics [32], space and cosmic-ray physics [33], nuclear facility research, and many other domains.

Using Geant4, it is possible to estimate also the dose in certain volumes of interest, and in the following Sections, various dose maps for a representative product of Copan are reported. More in detail, the product that has been modeled in the simulations is a swab in tube. Figure 2.9a shows a photograph of the single product. The CAD model of the product (Figure 2.9b) was imported into the Geant4 model using CADMesh [34], to achieve an accurate modeling of the product in the simulation, as shown in Figure 2.9c.

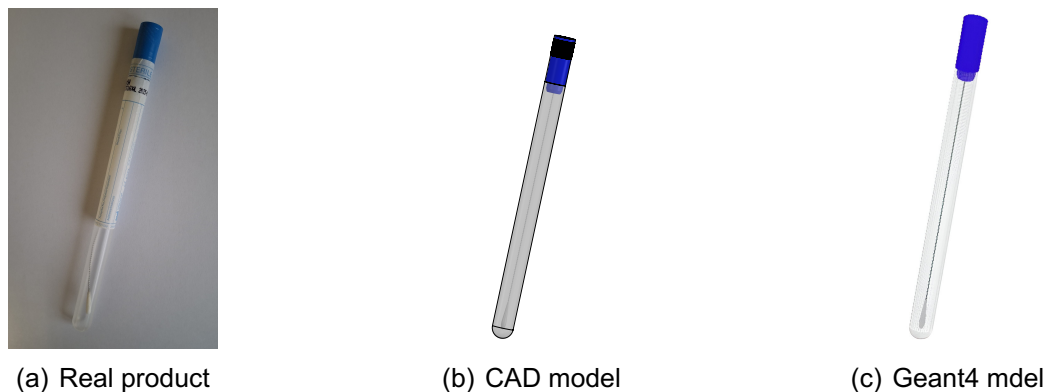


Figure 2.9: Swab in tube produced by Copan.

The product is packaged into small cardboard boxes, each containing 1'000 units. Ten of these boxes are then placed together in a larger shipping box. Figure 2.10a illustrates the complete geometry of the model used in the simulations, while Figure 2.10b presents an example of electron trajectories (shown as red lines) originating from a planar source positioned above the box and interacting with the products.

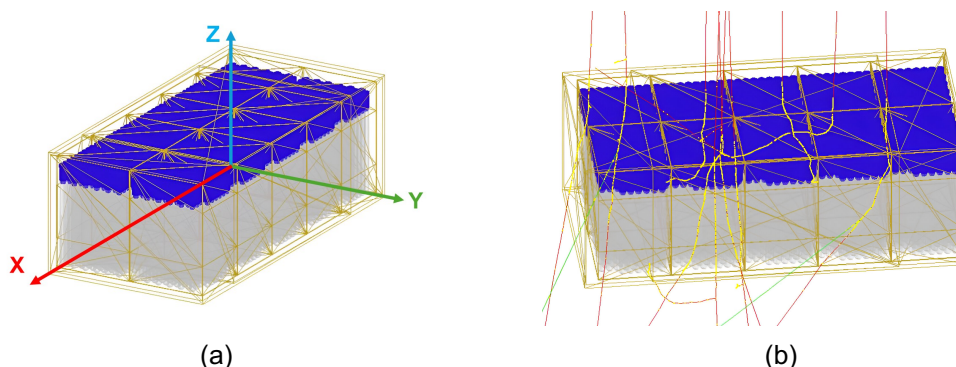


Figure 2.10: a) Geant4 simulation of a box containing swabs inside a tube. b) The box is irradiated with 10 MeV electrons (shown as red lines) emitted from a planar source positioned above it. Green lines represent X-rays produced by interactions between the electrons and the products, while each yellow point marks a location where an electron interacts with the products.

Two approaches in the estimation of dose inside the box of products were considered: the first is to divide the volume of the box into smaller volumes, called voxels, and to estimate the dose in each voxel. The second approach is to define small volumes inside the tube and to estimate the dose in each volume. In the following, the two approaches are presented and compared.

2.3.1 Dose Mapping Using Voxels

In Geant4 it is possible to define a parallelepiped mesh, which is a volume divided into smaller volumes called voxels, in which several quantities, averaged on that voxel, can be estimated, such as the absorbed dose, the energy deposited, the flux, etc. Figures 2.11, 2.12 report the energy deposited and absorbed dose maps for the box of products, with $310 \times 160 \times 120$ cubic voxels with a side length of 2 mm. The XY view shows the box from above, while the XZ view from the side, according to the reference frame shown in Figure 2.10. The plots show the dose (or the energy deposited) averaged on the dimension perpendicular to the view, and quantities are expressed in terms of Gy/primary (or MeV/primary). In fact, the estimated dose is divided by the

number of generated electrons—which are called primary particles—that are supposed to cross the box. The simulation was performed by generating 10^7 vertical (-Z direction) 10 MeV electrons uniformly from a planar source 390×690 mm in order to have at least 50 mm on each side of overscan on the box, whose dimensions are 275×565 mm.

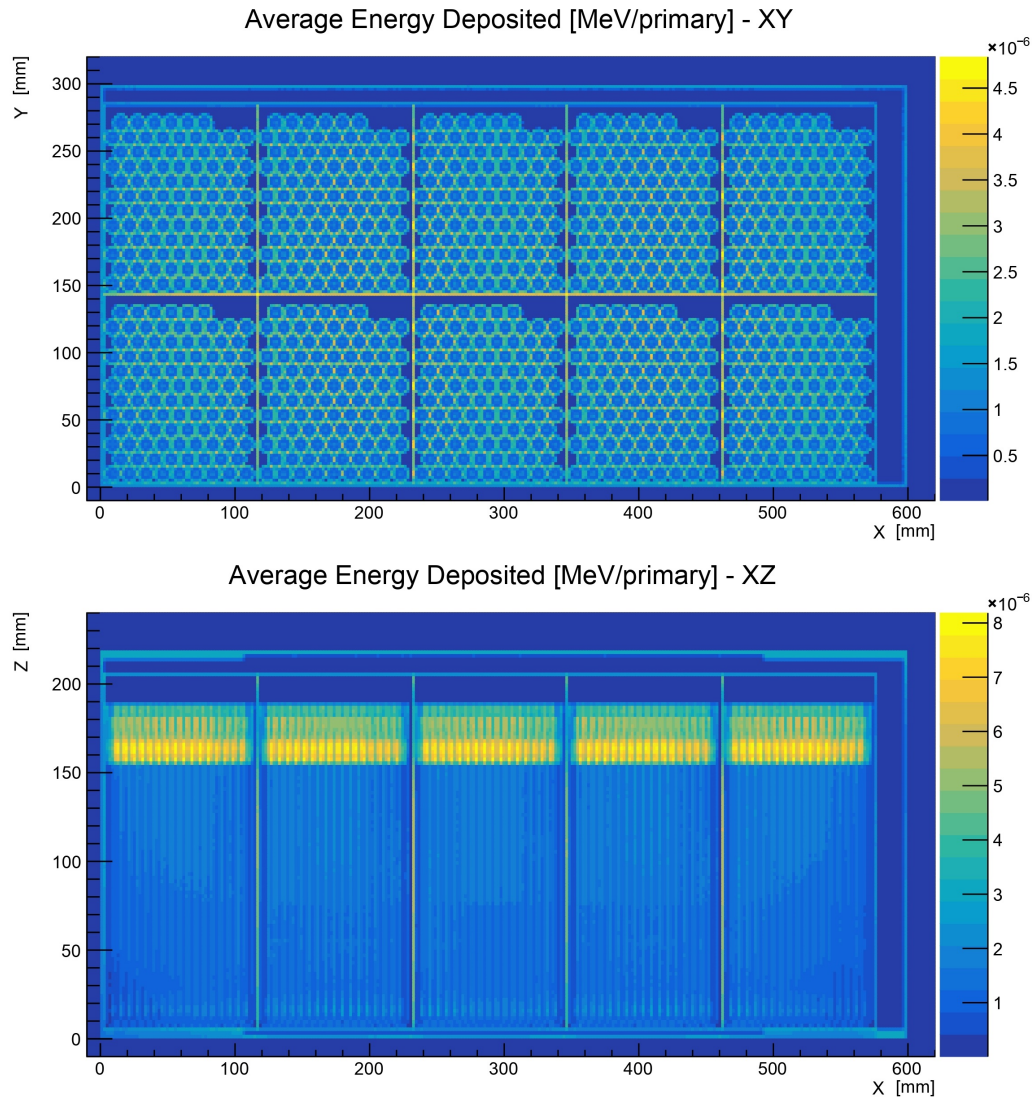


Figure 2.11: Deposited energy for a box of swabs in tube.

The energy deposition maps give an interesting "imaging" of the box, where it is possible to recognize the positions of swabs, the caps, and the boxes. As expected, the maximum energy deposition is on the caps, which are the most massive components.

The dose map reveals other interesting aspects: from the XY view, it is clear that products on the edges receive less dose with respect to the ones

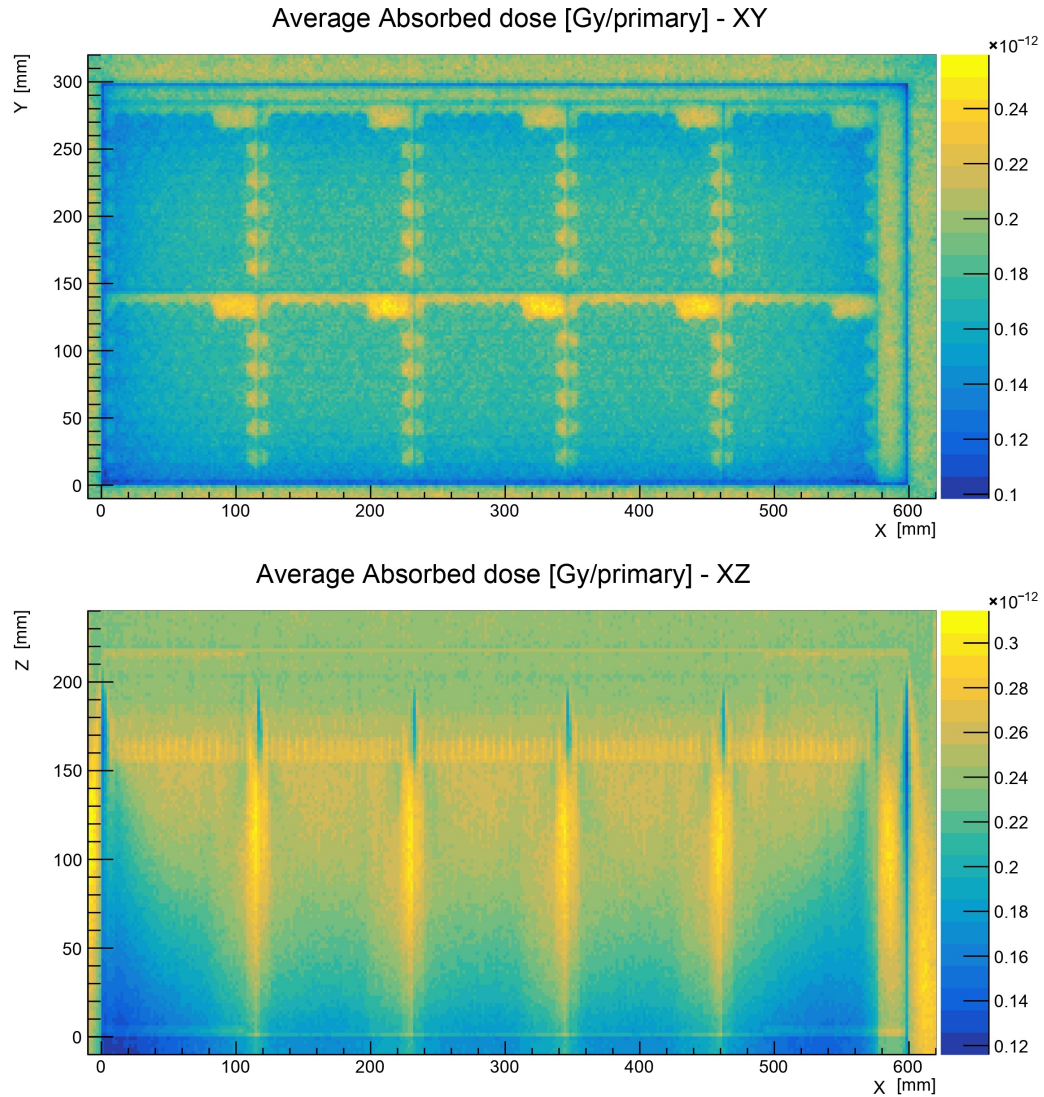


Figure 2.12: Absorbed dose for a box of swabs in tube.

in the center of the box. In fact, products in the center of the box receive electrons directly from the irradiation but also from the surrounding products, which scatter electrons. This last contribution is clearly lower for products on the edge of the box since the number of electrons scattered from the surrounding air to the box is much lower. The same dynamic also happens for secondary electrons produced in the interaction, and this explains the so-called edge effect. From the XZ view, the edge effect is even more evident. In addition, the dose is higher on the top with respect to the bottom; this is due to the fact that the fluence of electrons decreases with depth because of scattering and so the dose. Finally, regions with no products, as in between the small cardboard boxes, have higher dose because of the lower beam

attenuation.

Although the simulations revealed interesting and important aspects of the electron irradiation on products, it should be noted that the estimated doses are not expressed in terms of dose to water, which is the standard unit of measure for dosimeters used in radiation sterilization (ISO 11137-3 §4.1.2). This not only complicates the comparison with experimental results but also prevents direct comparison of doses at different locations within the box, as each voxel contains a unique mixture of materials that varies from one voxel to another. In principle, if all the voxels were of the same material, it would be possible to convert the dose in the material to dose to water (see Chapter 1), but this is clearly not the case, and so it is not straightforward to use these types of dose maps for estimating the DUR of the box, the irradiation time, the position of maximum and minimum dose, etc. For this reason, the next Section proposes another method that solves (although not completely) this problem.

2.3.2 Dose Mapping Using Sensible Volumes

Real dose maps are measured placing small dosimeters inside the products, in various positions inside the sterile barrier. The same approach can be applied to a simulation in Geant4. In Geant4, it is possible to define a "sensible volume" which can score various quantities, among which the energy deposited. The idea is to place sensible volumes of air inside each product, record the energy deposited, and finally obtain a dose map, where the dose in each swab is reported. Figure 2.13 reports the absorbed dose map for the box of products, obtained with the same simulation conditions reported in Section 2.3.1, and setting the full volume of air inside the tube as sensible volume.

The edge effects described in Section 2.3.1 are still evident, and in this case it is possible to compare doses at different locations within the box, as each sensible volume is the same. Assuming that the energy spectrum of the electrons that interact with the sensible volume doesn't change with the position, it is possible in principle to convert the dose into a dose to water, as described in Chapter 1. However, since electrons are not monoenergetic inside the box, it is difficult to assess the conversion factor, that varies with the energy of electrons. On the other hand, the conversion factor for air varies from 1.08 to 0.99 in the energy range from 2 to 10 MeV (see Chapter 1). Therefore, assuming that the dose in air is equal to the dose in water is a

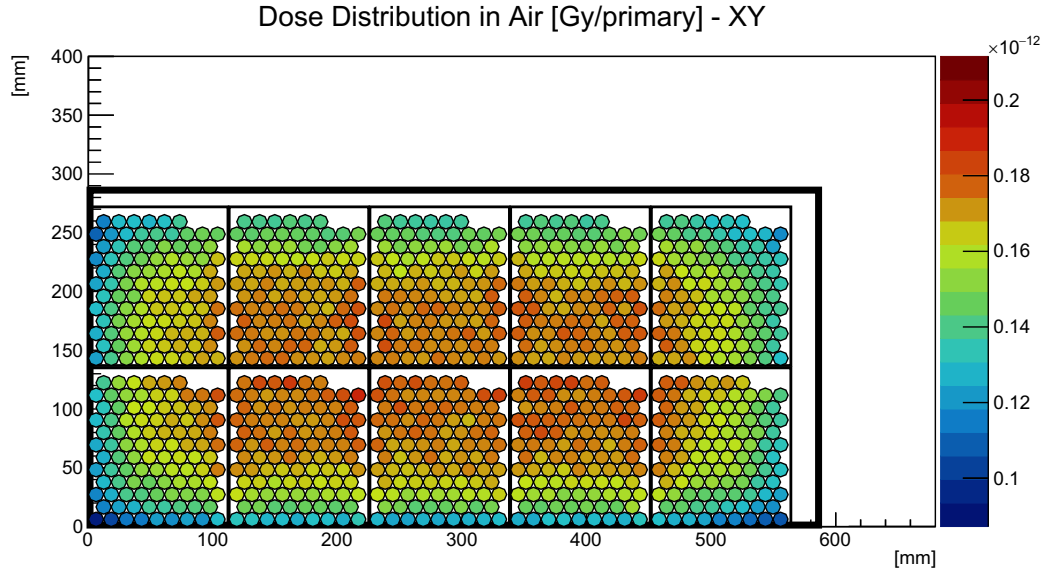


Figure 2.13: Absorbed dose map for a box of swabs in tube.

reasonable approximation, especially considering the simulation uncertainties that are discussed in the following sections.

Expressing the dose in terms of Gy/primary¹ allows estimating the conveyor speed required to achieve the minimum dose for the sterilization:

$$v = k \frac{I \cdot A_{box} \cdot (D/primary)_{min} \cdot NP}{D_{min} \cdot SW}$$

where:

- v is the speed of the conveyor [cm/s].
- I is the current of the beam [mA].
- A_{box} is the area of the box exposed to radiation [cm²].
- $(D/primary)_{min}$ is the minimum dose/primary (accounting only for the primaries that crossed the box) found in the simulation [Gy/primary].
- D_{min} is the minimum dose for the sterilization [kGy].
- k equals 6.24×10^{12} [1/C], which is related to the number of electrons that amounts to 1 Coulomb (6.24×10^{18} electrons = 1 C) and to other conversion factors (from kGy to Gy, from mA to C/s).

¹An equivalent formulation would be the dose per unit of fluence, where the fluence is calculated based on the number of primaries crossing the box. In the following, the unit dose/primary is used to avoid any ambiguity associated with the definition of fluence.

- NP number of passages under the beam.
- SW is the scan width [cm].

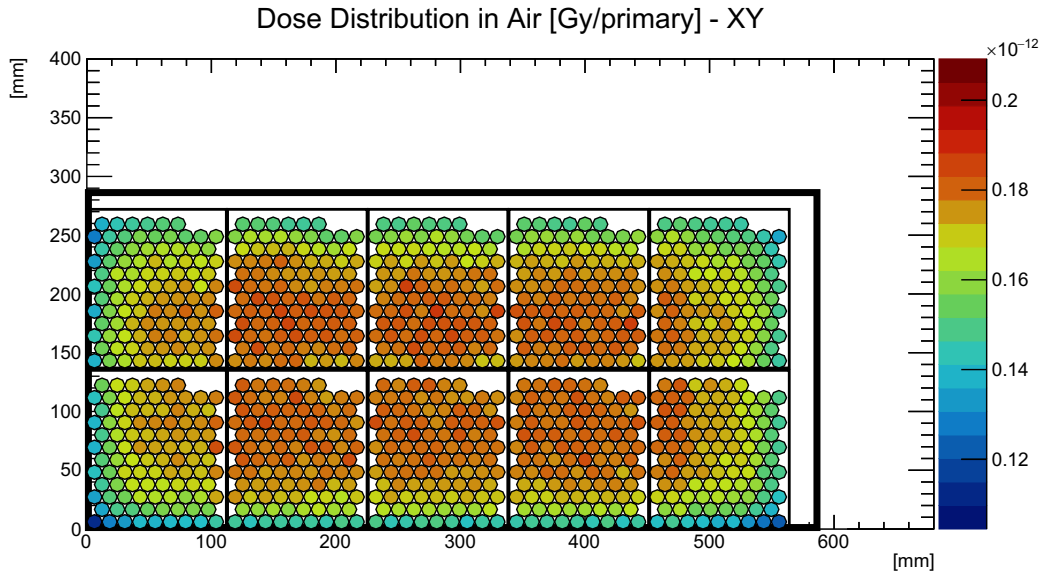


Figure 2.14: Absorbed dose map for a box of swabs in a tube, double irradiation.

Typically, products like the swab in a tube perform a double passage under the beam, and the second time the box is overturned, to improve the dose homogeneity. Figure 2.14 shows the dose map for a box irradiated with a double passage. To simulate the double irradiation, primary electrons are generated from two planar sources, one above the box and the other below.

With a single passage, $D_{min} = 9.69e-14$ [Gy/primary], $D_{max} = 1.92e-13$ [Gy/primary], $DUR = 1.98$, $D_{mean} = 1.63e-13$ [Gy/primary], while with a double passage $D_{min} = 1.16e-13$ [Gy/primary], $D_{max} = 1.90e-13$ [Gy/primary], $DUR = 1.64$, $D_{mean} = 1.73e-13$ [Gy/primary]. Considering the minimum D/primary of $1.16e-13$ Gy/primary, and assuming a current of 5 mA, a scan width of 80 cm, and a target dose of 25 kGy (typical for e -beam sterilization), the speed of the conveyor would be 5.6 cm/s, which is in the range of the possible speed of the Copan conveyor, i.e. from 3 to 20 cm/s. This means that for each passage, the box is irradiated for 10 s.

Until now, several aspects have been (on purpose) left out:

- Statistical uncertainty on results: Monte Carlo code estimations are affected by an uncertainty that is linked to the number of events that have been generated (i.e. the number of primary electrons generated).
- Product position uncertainty: products in the proposed simulation are placed according to a maximum packing configuration, that is not the real one.
- Sensible volume geometry: simulations were performed recording the dose in a sensible volume of the dimension of the void space in the tube, but this might hide effects that would be visible using smaller volumes of different shapes (e.g. dose gradients).
- Primary source: electrons are uniformly generated from a planar source, but in practice, they are emitted from the Rhodotron as the box of product moves under the beam.
- Physics model: simulations have been performed using QBBC_EMZ as physics list in Geant4, but many other physics models are possible.

The following sections will discuss in detail these points, and in the end, it will be possible to estimate the uncertainty (statistical and systematic) on the simulation related to these aspects. However, it should be noted that uncertainty values (also the statistical one) hold only for the presented type of simulation, with a swab in a tube packaged in the presented configuration. Changing product and packaging requires, in principle, a new estimation of the uncertainties; the following analysis aims at estimating the variability of results because of the systematic uncertainties more than precisely estimating the systematic uncertainty.

2.4 Dose Map Simulations Uncertainty

As previously mentioned, Geant4 is a Monte Carlo code, and it propagates a particle in matter sampling from probability distributions based on physical models. To estimate average properties of the radiation-matter interaction, as the Dose/primary, it is important to generate and transport a sufficiently large number of particles, since the statistical uncertainty on the average properties inversely scales with the number of particles generated. More precisely, since the uncertainty on an average quantity scales with $1/\sqrt{N}$, where N is the number of samples, in this case the number of samples is

related to the number of primaries generated, and so we expect that the uncertainty on the Dose/primary scales with $1/\sqrt{\text{primary}}$.

The statistical uncertainty is only a part of the total uncertainty on the simulations. In fact, the model in the simulation is only a numerical approximation of the real object, and so there are also systematic uncertainties related to the geometry, as well as on the physics model used in the simulation, and so on.

In the next Sections, all these uncertainties will be analyzed and estimated for dose simulations using sensible volumes.

2.4.1 Statistical Uncertainty on Simulations

The statistical uncertainty on the Dose/primary reflects the variability of the energy deposition process. For example, assuming that the deposited energy distribution is a Gaussian distribution, the uncertainty on the average dose can be easily estimated from the variance of the Gaussian. However, the energy deposition distribution in the sensible volume is far from being a Gaussian distribution, as shown in Figure 2.15. As expected, the deposited energy distribution is peaked for low energy contributions and decreases with energy.

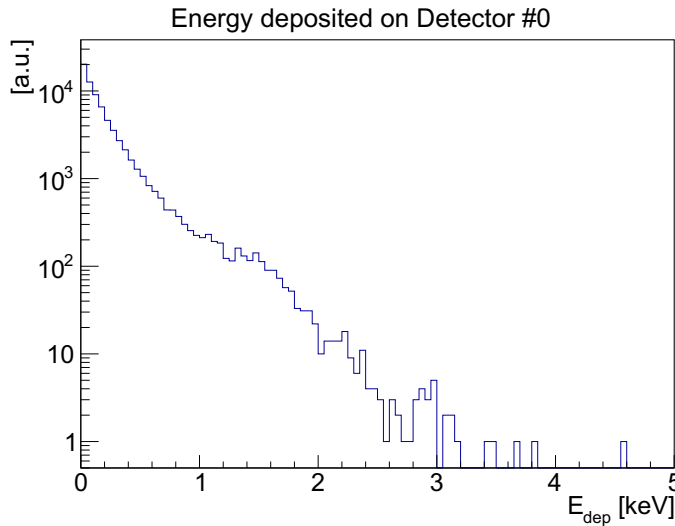


Figure 2.15: Energy deposited distribution on Detector #0, i.e. the sensible volume of air (9.188 cm³) inside the swab on the bottom left of Figure 2.14. Average energy deposited is 225 eV.

To estimate the uncertainty in the Dose/primary, a different approach must be adopted: the simulation should be repeated n times, each time us-

ing a different *seed* — that is, a different sequence of randomly generated numbers. As a result, each of the n simulations will produce different primary particles, leading to variations in the outcomes. However, average quantities such as the dose are expected to remain consistent. The uncertainty in the Dose per primary can then be evaluated by calculating the standard deviation of the n Dose per primary values obtained for each dosimeter. Thanks to the central limit theorem, these values can be assumed to follow a normal distribution. Figure 2.16 reports the Dose/primary averaged on the $n = 20$ simulations, and the error bars reflect its variability (1σ variation), as a function of the number of primaries (i.e. 10^4 , 10^5 , 5×10^5 , 10^6). The Dose/primary depends on the position of the sensible volume, and so the uncertainty: for this reason, Figure 2.16 reports two curves for two sensible volumes, one placed on the corner of the box, and the other in the center of the box. Increasing the number of primaries, the relative uncertainty (σ/μ) decreases, and in practice it seems that the relative uncertainty does not depend on the position of the sensible volume at high enough statistics (i.e. $\geq 5 \times 10^5$ primaries).

Figures 2.17, 2.18 report the average Dose/primary (averaged on the whole box) and the DUR in function of the number of primaries. The relative uncertainty on the average Dose/primary is a few percent already at the lowest number of primaries, while the DUR reflects the variability of the Dose/primary shown in Figure 2.16.

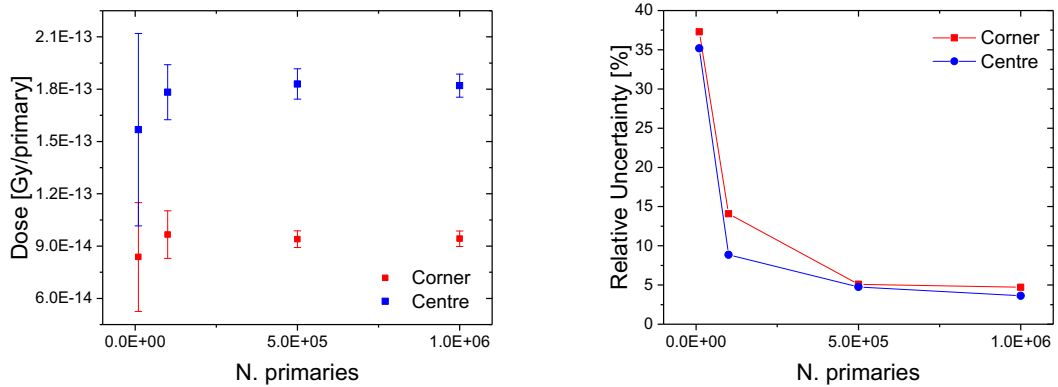


Figure 2.16: Average dose (left) and relative uncertainty (right) estimated repeating 20 times the simulation with different seeds on two different sensible volumes, i.e. one inside a product on the corner of the box, and another in the center of the box. Error bars are statistical only and correspond to one standard deviation.

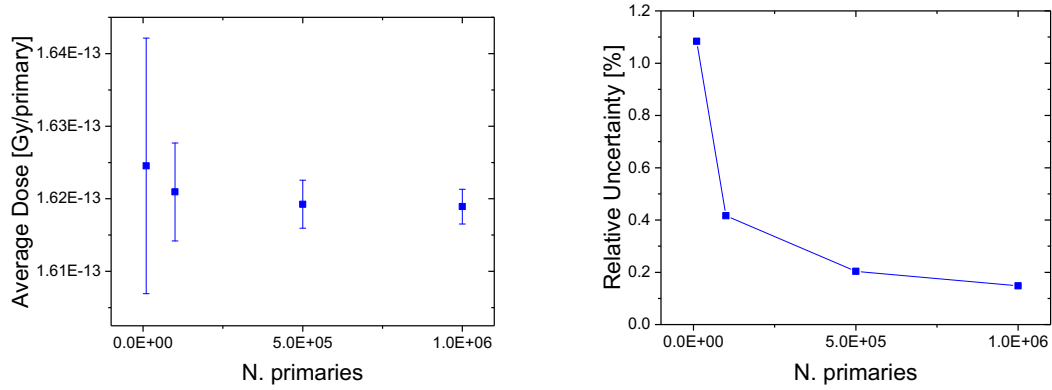


Figure 2.17: Average of the mean dose within the box (left) and relative uncertainty (right) estimated by repeating 20 times the simulation with different seeds. Error bars are statistical only and correspond to one standard deviation.

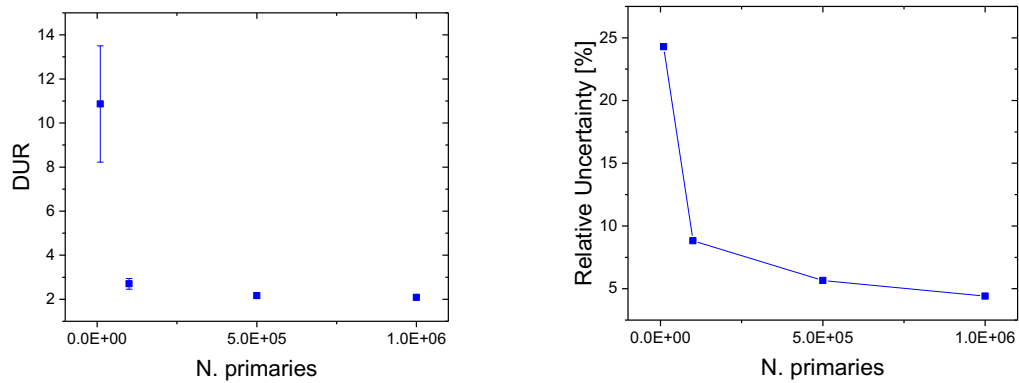


Figure 2.18: Average of the DUR (left) and relative uncertainty (right) estimated by repeating 20 times the simulation with different seeds. Error bars are statistical only and correspond to one standard deviation.

In all the cases, increasing the number of primaries has a benefit on the relative uncertainty, but this has, of course, an impact on the computational time that is almost linear, as shown in Figure 2.19, on a 12-core Intel Core i7-8700H @ 3.70 GHz PC (only 8 cores were used).

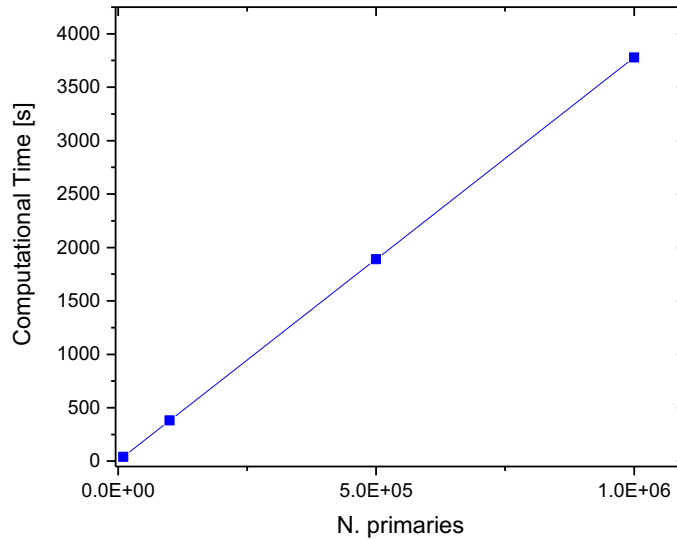


Figure 2.19: Computational time in function of the number of primaries

2.4.2 Systematic Effects on Simulations

Systematic uncertainties in simulations arise from the approximations that are necessary to describe and resolve a complex physical problem using a numerical model. More in detail, the main approximations for the simulations presented in this work come from:

- Geometry of the simulation: the model in the simulation is not the real box of products, and the sensible volumes are not the dosimeters placed inside the products.
- Physics of the simulation: the physical model used in the simulation is necessarily an approximation of the real-world physics.
- Source of primary particles: electrons are uniformly produced from a planar source; in practice, they are emitted from the Rhodotron as the product box passes beneath the beam.

In the following, the impact of these approximations is evaluated.

2.4.2.1 Geometric Approximations in the Simulations

In addition to the unavoidable approximations in the definition of the materials in the Geant4 model, and in the geometry of the products (CAD model is a mathematical description of the real product), the previous dose maps were performed assuming that products are placed inside the box following a configuration of maximum compaction. In practice, the free space available in the box allows the products to move, and so the real configuration inside the small box is more disordered, as shown in Figure 2.20.



Figure 2.20: Configurations of products inside the small box. Some blue caps are missing only for visualization purposes.

In some areas of the box, products are really arranged in a configuration of maximum compaction, but generally they are positioned following a more disordered pattern. Figure 2.21 reports the dose map with products placed inside the small box in a manner analogous to the configuration depicted in Figure 2.20. Only 88/100 of the products were placed inside the box in the simulation without overlaps, because in reality products and boxes are deformable objects, and this allows for more random configurations that are not possible in the simulation model without introducing overlaps.

The effect of the different configuration of products is shown in Figure 2.22, where the dose distribution inside the box of product is represented as a box plot. The "ordered" scenario refers to the dose map where products are placed according to the maximum compaction configuration (Figure 2.13),

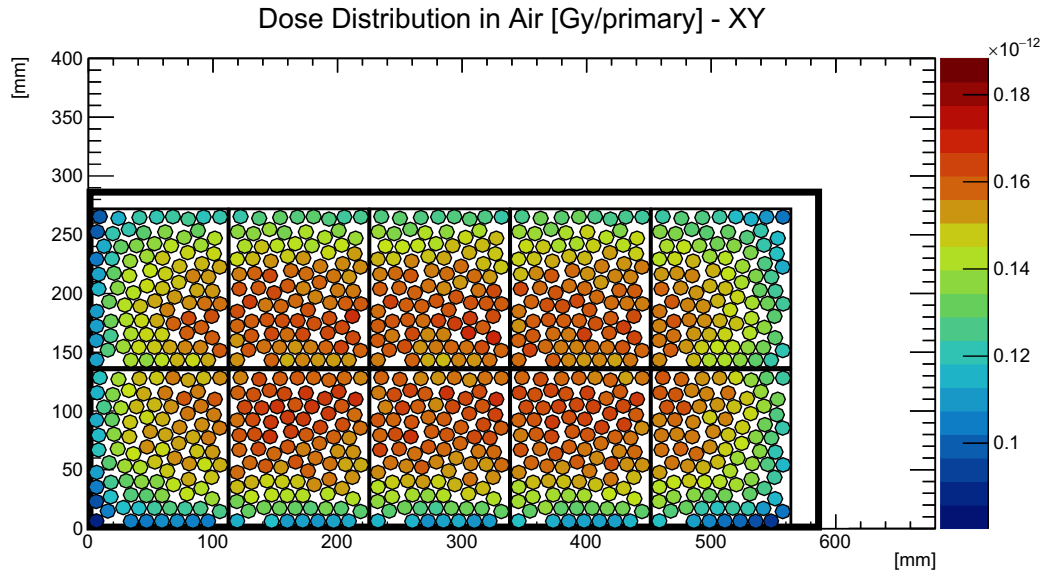


Figure 2.21: Absorbed dose maps for a box of swabs in a tube following the arrangement shown in Figure 2.20.

while the "disordered" scenario refers to the dose map reported in Figure 2.21, where products are placed according to the configuration shown in Figure 2.20.

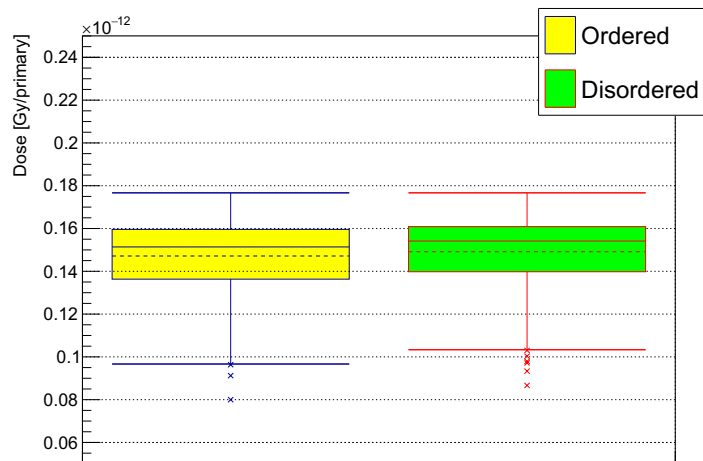


Figure 2.22: Dose distribution comparison between "ordered" scenario (products placed according to the maximum compaction configuration), and "disordered" scenario (products are placed according to the configuration reported in Figure 2.20)

The continuous line within the box represents the median of the dose distribution, the dashed line its mean. The upper and lower sides of the rect-

angle are the upper (Q3) and lower (Q1) quartiles, meaning that 75% of the data points are less than Q3, and that 25% of the data points are less than Q1. The whiskers represent the part of the distribution not covered by the box: the maximum length of whiskers is set to 1.5 times the interquartile range, and any points outside the whiskers are represented by crosses.

Both simulations are performed generating more than 10^6 primaries (i.e. 4×10^6 primaries); therefore the expected relative uncertainty on the single value of the dose is less than 5%, and less than 0.2% on the average dose. Although it cannot be excluded that the difference in minimum dose and DUR of 6.8% and 7.6% respectively is due to statistical fluctuations, the difference in the average dose of 1.3% is statistically significant, as well as the narrower interquartile range for the disordered configuration, suggesting that the latter one has a more uniform dose distribution.

Another approximation on the model is using a sensible volume that completely fills the volume of air inside the tube. Estimating the dose on such a "big" volume smears dose gradients that might be important for the sterilization process, i.e. some points inside the sterilization volume might not reach the sterilization dose, although the mean dose inside the whole product is higher than the sterilization dose. However, it is possible to use smaller scoring volumes placed at various points inside the sterilization barrier, but this leads to a lower number of events collected inside the volume, and so a poorer statistic and a higher relative uncertainty for the same number of generated primaries. Figure 2.23 shows the dose distributions scored inside a "film" sensible volume (10 x 1 x 6.76 mm) and a "disc" sensible volume (outer diameter 10 mm, inner diameter 3.73 mm, height 1 mm) placed at three different heights along the swab, as shown in Figure 2.23. Simulations were performed generating $1E7$ primaries, with double passage irradiation (same configuration as Figure 2.14). The volume of the film and the disc amounts to 0.0676 cm^3 , while the volume of air inside of the swab amounts to 9.188 cm^3 , therefore, the number of events scored in the smaller volumes will be with a good approximation $0.0676/9.188 = 0.007$ times the number of events scored in the "full" volume, and so the relative uncertainty on the Dose/primary, DUR and average dose in the disc or film volume with a simulation of $1E7$ primaries corresponds to the uncertainty for a simulation with $0.007 \times 1E7 = 7E4$ primaries using a full sensible volume inside the swab. Referring to Figure 2.17, the uncertainty on the average dose on the box using films and discs amounts to approximately 1%, while the uncertainty on

the dose values and on the DUR amounts to $> 15\%$ and 10% respectively (see Figures 2.16, 2.18).

Simulation results show that the average dose absorbed by the film is consistently higher than that measured by the disc. Furthermore, among the three defined sensitive volumes within the product, the dose recorded in sensitive volume no. 3—located directly beneath the swab's cap—is the highest. This is followed by sensitive volume no. 2, and finally by sensitive volume no. 1, which receives the lowest dose. This gradient in dose deposition aligns with expectations for double-sided irradiation. Specifically, when the products are irradiated from the bottom (tip) upward to the top (cap), the dose distribution across the three sensitive volumes tends to be more uniform. In contrast, when irradiation is performed from the top (cap) downward to the bottom (tip), a more pronounced dose gradient is observed. This is due to the fact that the cap, being denser than the surrounding material, is the first structure encountered by incoming electrons. As a result, the beam undergoes increased scattering and attenuation, leading to a broader spread and a significant reduction in electron flux deeper in the product, particularly at position 1. This effect is clearly illustrated in Figure 2.24, where the differences in dose deposition between the two irradiation directions are depicted.

In conclusion, the maximum discrepancy between film, disc and entire volume, placed at various heights, is approximately 6% on the average dose, and the average dose calculated over the entire volume of the product falls within the range defined by the average doses measured using the film and disc sensitive volumes.

2.4.2.2 Physical Approximations in the Simulations

Geant4 offers various reference physics lists, which are routinely validated and updated with each release. In particular, for the electromagnetic physics, there are ten available extensions, and in the following four different physics list are compared: three of them are variations of the "QBBC" physics list, which is recommended for medical and space physics simulation [35], and one is the "LHEP" physics list, which is one of the fastest of all physics lists. More in the details [36]:

- QBBC_EMZ: QBBC physics list with EMZ extension of the electromagnetic physics. EMZ offers the best set of electromagnetic physics models selected from the low energy and standard packages, but at the cost of a high computation time.

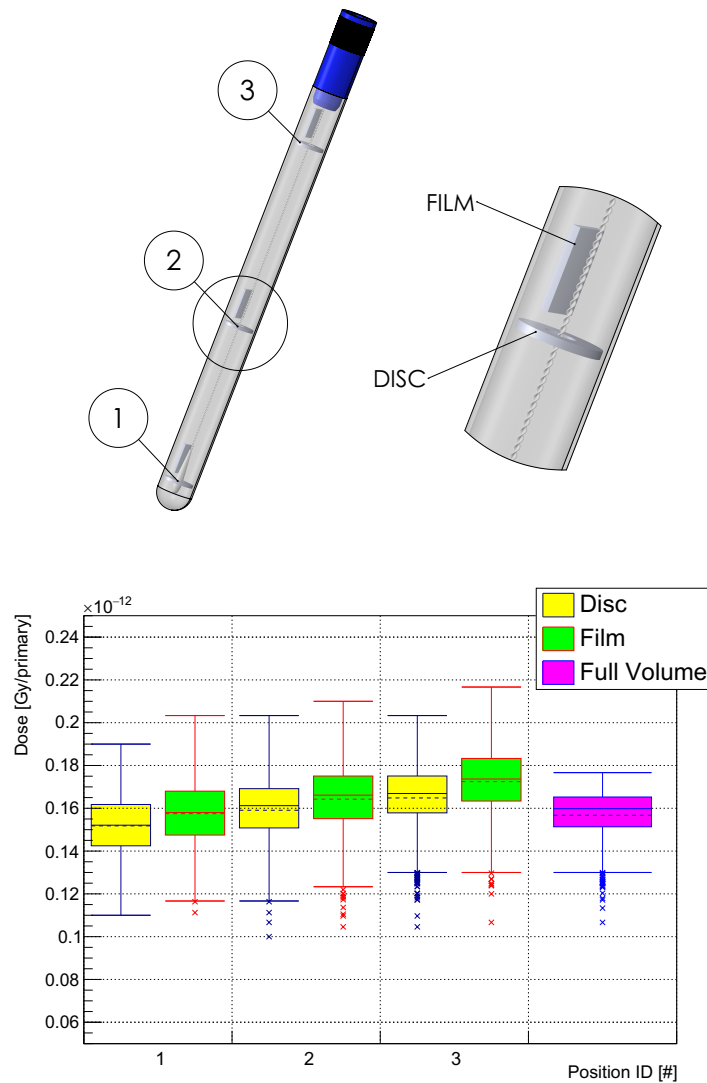


Figure 2.23: Dose distribution comparison between three simulations: one with disc sensible volumes, one with film sensible volumes, and one with sensible volumes that completely fills the volume of air inside the tube. Film and disc volumes are placed at different heights along the tube.

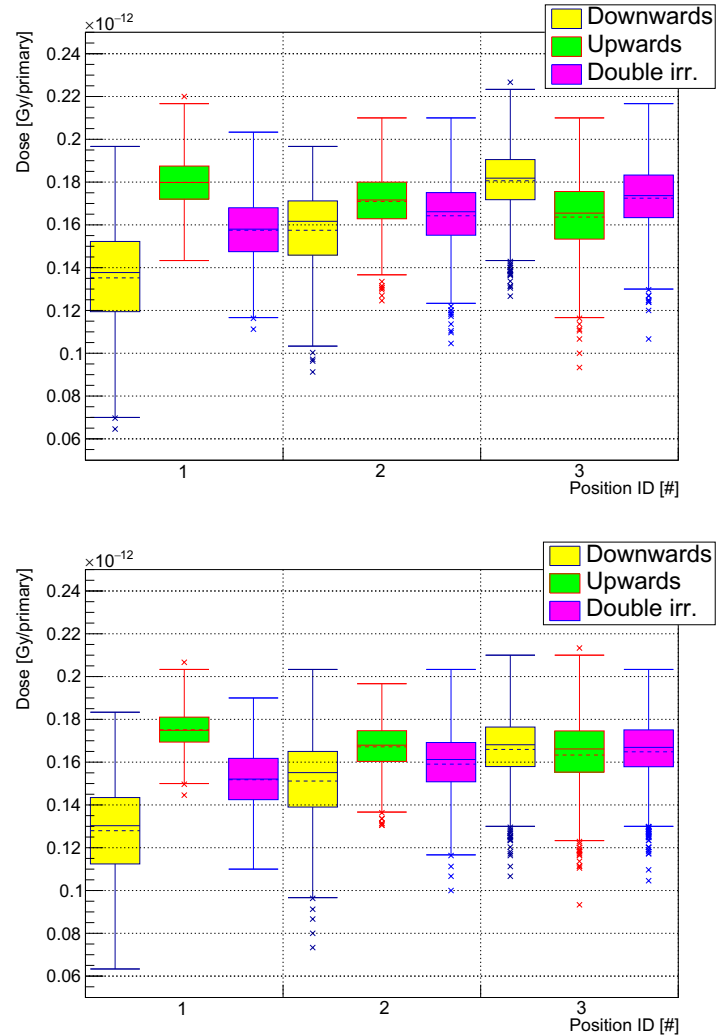


Figure 2.24: Dose distribution comparison between irradiation downwards, upwards, and double irradiation with (top) film sensible volumes and (bottom) disc sensible volumes. Film and disc volumes are placed at different heights along the tube.

- QBBC_EMV: QBBC physics list with EMV extension of the electromagnetic physics.
- LHEP: LHEP physics list with the standard electromagnetic model.
- QBBC_PEN: QBBC physics list with PEN extension of the electromagnetic physics. PEN uses Penelope-2008 set of models in substitution of standard models for gamma, electrons, and positrons.

Figure 2.25 shows the dose distributions using the four physics lists previously described. Simulations were performed with $1E7$ primaries (downwards, dose on the full volume inside the product).

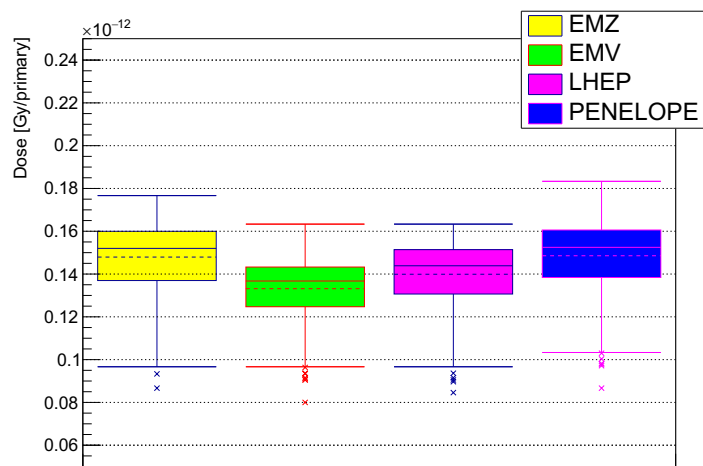


Figure 2.25: Dose distribution comparison between simulations with four different physics lists.

The differences in the average dose, with a maximum 11%, are statistically significant, as well as the minimum and maximum doses, which reflect a maximum variation in the DUR of 8%. Finally, the difference in time of simulations is also significant: EMV, EMZ, and PEN are 87%, 43%, and 53% slower than the standard electromagnetic model.

2.4.2.3 Electron Source Approximation in the Simulations

During the sterilization process, the box of products is moving along the conveyor, and the beam of electrons is scanned along the perpendicular direction of the conveyor. In addition, the beam is deflected by a pseudo-parallel magnet such that it always impinges on the product (almost) perpendicularly

to the box. The speed of the conveyor and the scanning frequency are such that electrons are uniformly distributed in the box, and so the uniform planar source approximation would be valid. In practice, electrons do not follow exactly a uniform distribution in space. Figure 2.26 compares the dose distribution in the box of product with electrons generated from a planar source and electrons generated following the distribution of electrons given by the combined motion of the box under the conveyor and the scanning of the beam, i.e. a zig-zag pattern on the box. For the latter simulation, standard values for the scanning frequency, duty cycle, and speed were assumed to be 50 Hz, 50%, 3.3 cm/s. The beam was represented as a 2D Gaussian profile, and its orientation is also defined by an angle sampled from two Gaussian distributions.

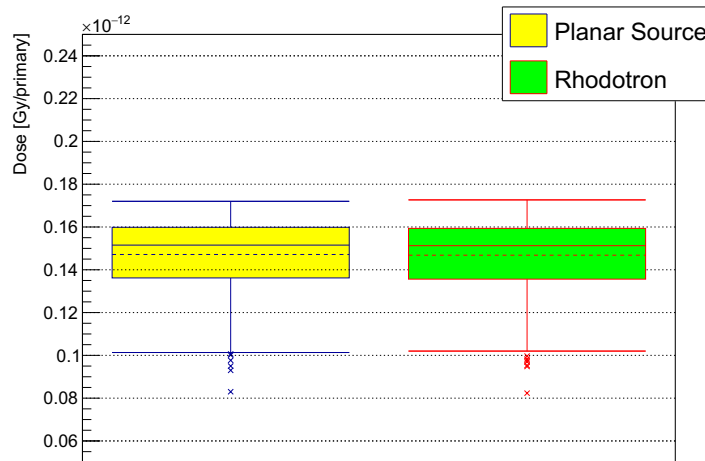


Figure 2.26: Dose distribution comparison between a simulation with a planar source of electrons, and a simulation with a spatial generation of electrons more similar to the one from the Rhodotron combined with the motion of the boxes.

In this comparison, the differences between the two distributions are not statistically significant, and so the planar source provides a good approximation of the real distribution of the beam.

Another approximation in the simulation is the omission of the 40 μm -thick titanium window at the beam scan exit, which may affect the electron energy spectrum, their angular distribution, and the generation of X-rays. Figure 2.27 compares the dose distribution in the box of product with electrons generated from a planar source with and without the titanium window

below the planar source, and the effect of the titanium window results being not relevant.

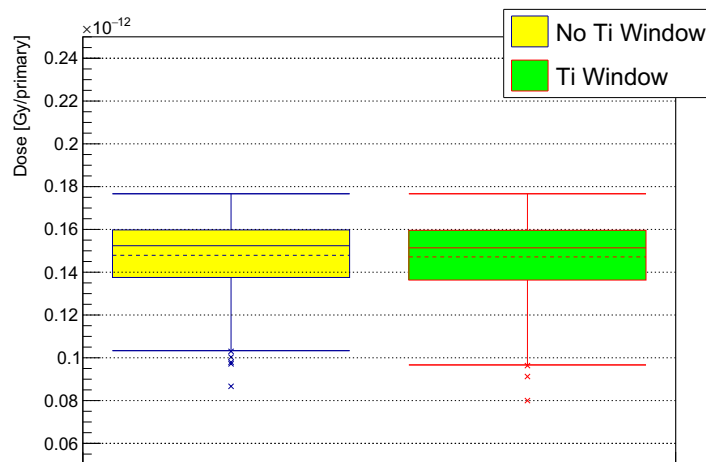


Figure 2.27: Dose distribution comparison between two simulations with and without the titanium window below the source plane.

Finally, the monochromatic approximation of the beam is evaluated: the electron beam from the Rhodotron is very narrow in energy, with a peak in the spectrum at 10 MeV and an energy spread tolerance of a few hundred keV. Figure 2.28 compares the dose distribution in the box of product with electrons generated from a planar source and titanium window with an initial energy of 10 MeV and 9.75 MeV. The difference in energy results in two dose maps that do not differ, except for statistical fluctuations.

2.5 Irradiation Setup Optimization

As discussed at the beginning of the Chapter, it is important to achieve uniformity of the dose inside the box of products in order to achieve the sterilizing dose in all products without exceeding the maximum dose tolerable for the product. Without changing the packaging of the products, which might require considerable effort from the production point of view, several precautions can be applied to increase dose uniformity [37–39]:

- Box positioning with the denser part on the bottom (when single irradiation).
- Beam scan modulation and optimization of the pseudo-parallel angle.

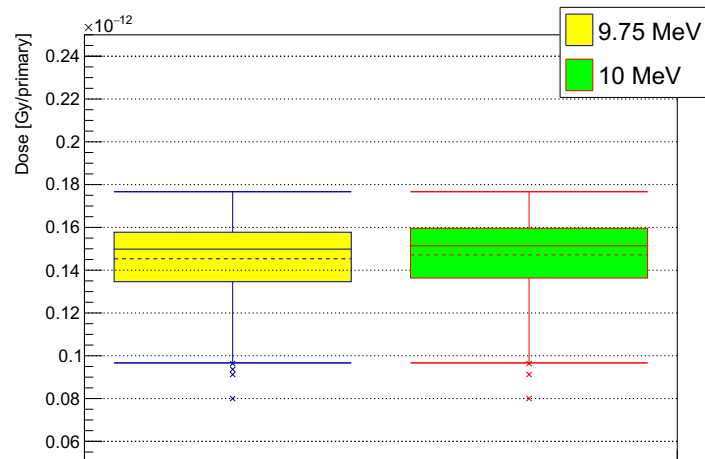


Figure 2.28: Dose distribution comparison between two simulations with primary electrons generated at 10 MeV and 9.75 MeV.

- Overscan and irradiation of a continuous row of boxes.
- Scattering plate.

The impact of these measures and adjustments is evaluated in the following.

The box positioning under the beam is relevant when the irradiation is performed in only one passage (or an odd number of passages). As shown in Section 2.4.2.1, when products are irradiated with the cap (the denser part of the product) on the bottom of the box, i.e. the "upwards" irradiation, the dose distribution is more uniform, since the beam penetrates more in the box before being scattered out of the box by the denser region. The difference in the DUR in the two cases is significant, from 3.1 with the beam downward to 2.2 with the beam upward using the disc sensible volume, and from 3.5 to 2.4 using the film sensible volume. Therefore, a significant improvement in homogeneity can be easily reached by positioning the box with the denser part at the bottom whenever possible.

Improved uniformity can be achieved with an optimized beam modulation: slowing down the scanning speed of the beam close to the edges of the box of product can improve the DUR, as more electrons are impinging on the box where the dose is lower because of edge effects. However, the beam modulation is performed by changing the function of the current in the scanning magnet, and this might not be accessible to the accelerator user. Furthermore, the pseudo-parallel magnet may be tuned to divert electrons

that would otherwise go out of the box, but this is also limited by the accessibility to the user.

Another crucial factor for uniformity is the overscan, which represents half the difference between the beam scan width and the box width—in other words, the extent to which the beam extends beyond the box. Of course, the overscan cannot be zero because of the uncertainty of the position of the box under the beam, but also because electrons that do not impinge on the box may be scattered towards the box, delivering a dose especially on the sides of the box. In addition, primary electrons that interact with the surrounding air generate secondary electrons that give a dose to the products. Figure 2.29 compares the dose distributions in the box of products with different values of overscan.

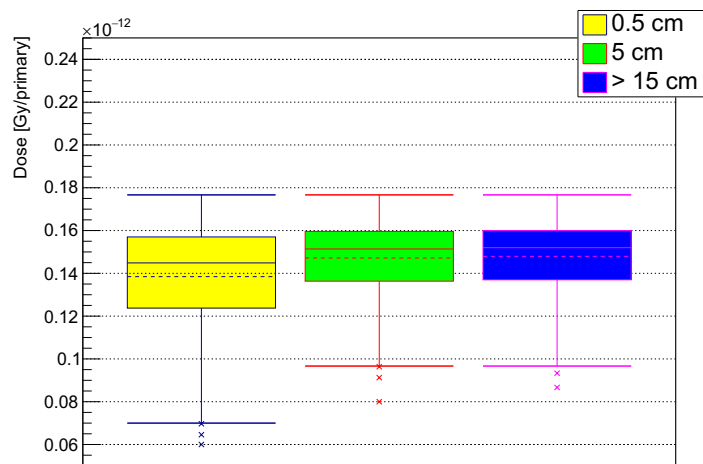


Figure 2.29: Dose distribution comparison between three simulations with different values of overscan.

For an overscan value of 0.5 cm, the minimum dose is sensibly lower with respect to an overscan of 5 cm, and the distribution with an overscan of 15 cm is essentially the same as with 5 cm, suggesting that further increasing the overscan does not lead to a more homogeneous dose, but only a longer irradiation treatment.

Edge effects are also reduced by the surrounding boxes of products because of the electrons that scatter out from the boxes nearby. The effect is clearly shown by the dose map in Figure 2.30, which comes from a simulation of a box of products with two adjacent boxes on the two long sides of the box ($1E7$ primaries downwards). In fact, this configuration is more realistic than that of a single box, as sterilization plants typically irradiate a continu-

ous line of product boxes, and a dedicated system pushes the box under the beam such that no void spaces are left in between one box and the following.

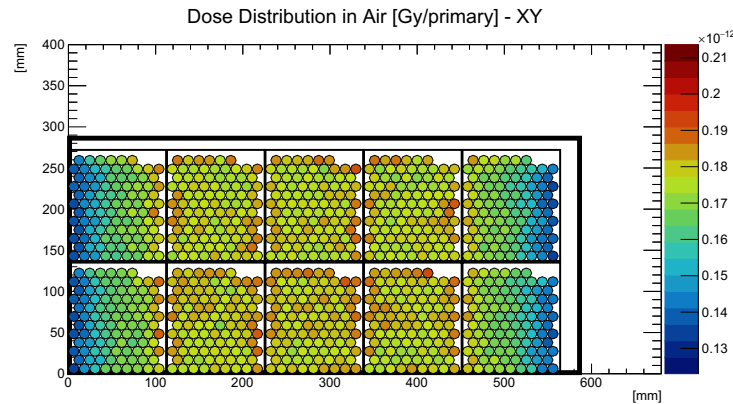


Figure 2.30: Absorbed dose map for a box of swabs in a tube with two adjacent boxes on the two long sides of the box.

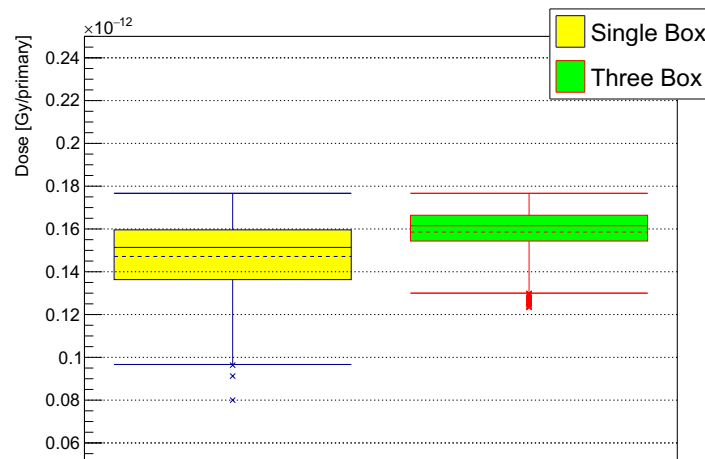


Figure 2.31: Dose distribution comparison between a simulation with a single box and a simulation with a box of products with two adjacent boxes on the two long sides of the box.

The difference in the dose distributions is significant, as shown in Figure 2.31: the DUR goes from 1.98 to 1.42, and the average dose is 8% higher.

Finally, the DUR can be effectively reduced through the use of a "scattering plate": by placing a thin sheet of high-density material between the electron beam horn and the product box, the energy dispersion (or straggling) of electrons is enhanced, leading to improved radiotreatment quality

both at the surface and at depth [40]. The scattering plate serves a dual purpose:

- The plate scatters the electrons, and so the fluence decreases, but some electrons that would not reach the box are directed toward the sides of the box, reducing the edge effect.
- Electrons lose energy crossing the plate, and so the energy spectrum is broadened and the stopping power increases.

The scattering plate technique has been investigated in collaboration with Aerial (Illkirch-Graffenstaden, France) and IBA (Louvain-La-Neuve, Belgium) on a specific Copan product composed of a swab and a tube with a gel inside, as shown in Figure 2.32. This product is particularly challenging for the electron sterilization, because of its dis-homogeneity and presence of the gel. Through simulations, it is possible to estimate the benefit of the scattering plate.

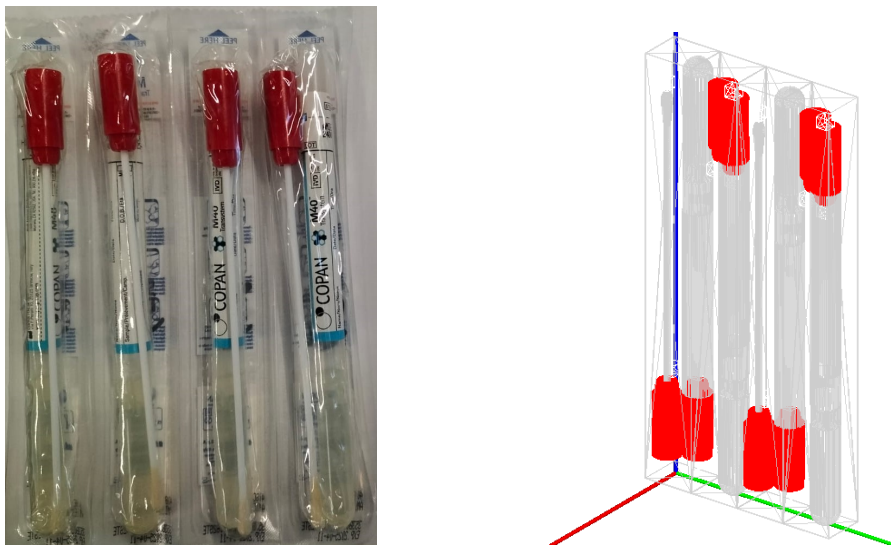


Figure 2.32: Swabs and gel-containing tubes manufactured by Copan irradiated at the Aerial center in Illkirch-Graffenstaden, France, both with and without the use of a scattering plate. The irradiation was carried out in collaboration with IBA (Louvain-La-Neuve, Belgium).

However, the product also presents challenges for simulation efforts. In fact, each tube and swab is packaged into a pouch, and then a strip of 50 pouches is placed inside a thin, aluminized bag. Eight bags are then placed inside a box. The G4 model is shown in Figure 2.32: inside each pouch, which is the sterilization barrier, five sensible volumes of air are placed to

score the dose absorbed in the product. The scattering plate was modeled as a 1 mm-thin sheet of copper 110×80 cm, placed at 10 cm above the box of products.

From double irradiation simulations (using $5E7$ primaries for each irradiation), the minimum dose is recorded in both cases in the sensible volumes inside the gel, and the maximum dose in the sensible volume close to the cap. It turns out that the scattering plate reduces the DUR on the product from 1.92 to 1.44, but also the surface dose is sensibly reduced because of the scattering plate, of about 20%, that leads to a higher irradiation time. However, the benefit of homogeneity is significant.

The challenges related to the scattering plate are primarily engineering in nature. Specifically, the metallic plate tends to become very hot, and if it is mounted beneath the beam scanning horn, it must be adequately cooled. An alternative approach is to design trays with the scattering plate integrated on top. However, in this configuration, the tray must be sufficiently large to ensure the scattering plate produces the desired effect; otherwise, only a minimal number of electrons will be redirected toward the sides of the box.

Radiation Effects on Polymers

When ionizing radiation interacts with microorganisms, the deposited energy can cause their inactivation: this process is at the basis for sterilization using ionizing radiation. On the other hand, the interaction can also induce various side effects on the products under sterilization, which might alter the functionality of the device itself. Many medical devices, and specifically all the devices produced by Copan, are made of polymers, and the exposure to radiation might lead to embrittlement of the material and degradation of mechanical properties. For this reason, it is crucial to test and evaluate the effect of ionizing radiation prior to sterilization.

The effect of radiation on products depends on various irradiation parameters, such as the dose level, the irradiation temperature, the dose rate, and the oxygenation of the product, but also on product characteristics such as the geometry, the material, and the manufacturing process [41, 42]. To generalize the study of the radiation effects, it is therefore necessary to study the raw materials and eventually focus on specific designs.

Since polymeric materials for 3D printing are of increasing interest for applications and prototyping in the medical field [43–45], the following sections evaluate the effects on various categories of commercial 3D printing materials and report experimental studies on the printing filament. Most of the results are also presented in a scientific paper published in the *Journal of Physics: Materials* of which the author of this thesis is the first author [46]. Before presenting the study's results, an overview of the physics behind radiation-induced effects on polymers is provided in the next section.

3.1 Physics of Radiation Induced Effects on Polymer

A polymer is a material that has a large molecular structure composed of chains of many repeating units called monomers ("poly" and "mer" mean "many" and "parts" in Greek). Polymers are widely used in different industries as plastics and resins; in fact, plastics are polymers with additives and are based on long-chain molecules developed from alkenes [47].

The mechanical and chemical properties of the polymer strongly depend on the chemical structure of the monomers and the configuration of the chains. Chains can be arranged in an ordered configuration, defining a so-called "crystalline" structure, opposed to the amorphous structure where chains are displaced in a disordered manner. Many polymers, such as polyethylene (PE) and polypropylene (PP), have a semicrystalline structure, i.e. present both amorphous and crystalline areas, with a percentage described by the degree of crystallinity. Crystalline areas exhibit a melting transition at the melting temperature (T_m), at which aligned chains turn into a randomly oriented viscous liquid, while amorphous areas are characterized by the glass transition at the glass temperature (T_g), at which the material changes from a hard and brittle state into a molten or rubber-like state [48].

The ionizing radiation induces excitations and ionizations of the polymer chains, leading to the formation of free radicals and ions that react, resulting in mainly two competing dynamics that occur simultaneously [41, 49]:

- Cross-linking: the formation of new bonds in between the polymer chains, typically leading to an increase of the elastic modulus and strength and to embrittlement of the material. Slightly cross-linked polymers are called "elastomer", and are characterized by high and reversible deformability.
- Chain scission: reduction in molecular weight and consequent degradation of the mechanical properties of the polymer, usually losing in strength and elongation at break.

The radical's lifetime depends on its mobility, which in turn depends on the amorphous/crystalline area, and its reactivity (the type of radical): radicals are typically generated in a few nanoseconds and react very quickly, although some radicals exhibit long lifetimes (days to weeks), especially in the

crystalline phase, where radicals have less mobility. For this reason, polymers with a high degree of crystallinity are more radiation resistant[50].

The predominance of crosslinking or chain scission is expressed quantitatively by the radiochemical yield, which is the number of molecules formed or changed for 100 eV of energy absorbed. Table 3.1 summarizes the G-values for crosslinking and chain scission for some common materials in the medical field: LDPE, HDPE and PB are among the most crosslinkable materials. Interestingly, the HDPE, which has a high crystallinity degree, is less prone to crosslinking than LDPE, since the higher crystallinity reduces the mobility of chains. On the other hand, PMMA, PTFE result in being degradable materials due to the high G-value for chain scission. Polystyrene is the most resistant polymer among the ones reported in the table, and Figure 3.1 reports a further overview on the radiation stability of common medical polymer families.

Polymer	Acronym	Crosslinking	Chain Scission
Low-density polyethylene	LDPE	1.42	0.48
High-density polyethylene	HDPE	0.96	0.19
Isotactic polypropylene	iPP	0.16-0.26	0.29-0.31
Atactic polypropylene	aPP	0.4-0.5	0.3-0.6
Poly(methyl methacrylate)	PMMA	<0.50	1.1-1.7
Poly(tetrafluoroethylene)	PTFE	0.1-0.3	3.0-5.0
Polystyrene	PS	0.019-0.051	0.0094-0.019
Polybutadiene	PB	5.3	0.53
Polyisobutylene	PIB	0.05-0.5	5
Butyl rubber	IIR	<0.5	2.9-3.7

Table 3.1: G-values for crosslinking and chain scission for some common polymers [51].

As discussed in Chapter 1, the interaction mechanisms of gamma and X-ray radiation lead to similar effects as that of an electron beam, i.e. the formation of secondary electrons, which ultimately leads to heating of the material and chemical reactions. As a result, the effects on a material exposed to electrons, gamma rays, or X-rays are similar. For this reason, tests with X-rays allow the study of the radiation tolerance of materials exposed

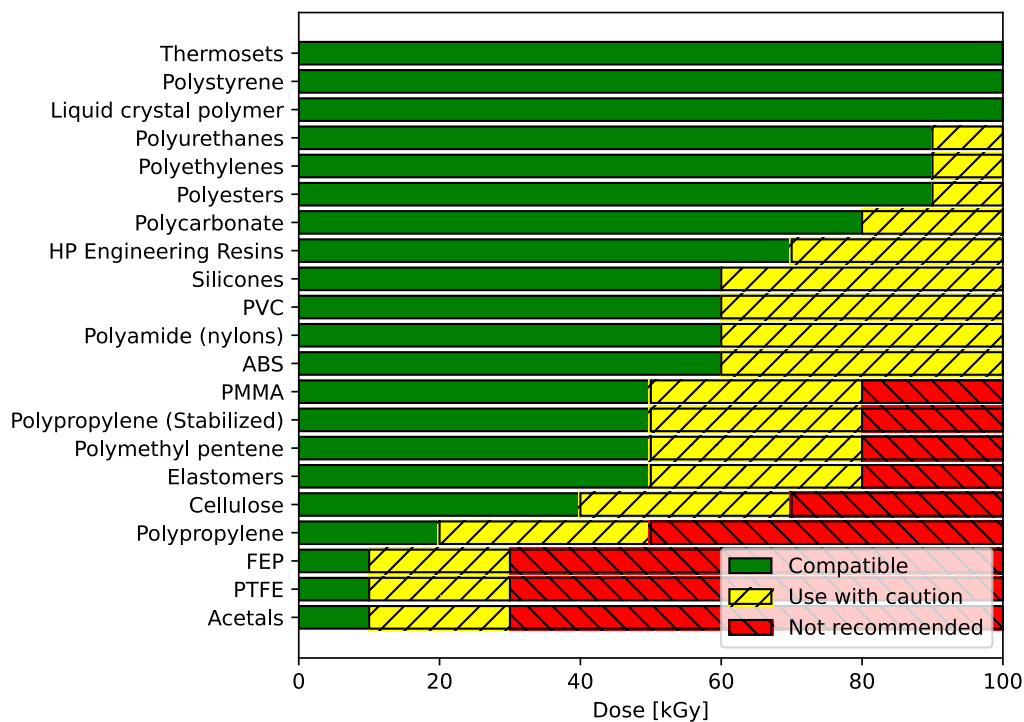


Figure 3.1: Relative radiation stability of common polymers [52].

also to other types of radiation sources, with the advantage that low-energy X-rays can be easily produced by using commercial X-ray tubes.

The difference between the different types of radiation is more related to the radiation source and, more precisely, to the typical dose rate, which in general has an impact on the material effect. Dose rate effects are related mainly to oxidation: the lower dose rate allows the oxygen diffusion in the bulk of the material, which is therefore continuously exposed to oxygen and so more prone to oxidation of the polymeric chain, which often leads to chain scission. Of course, this effect is more important for thin products such as films. Finally, the different dose rate has an impact on the irradiation temperature: although T_g and T_m are rarely reached during irradiation, a higher temperature increases the mobility of radicals and so the induced effects.

In the following, the effects in a selection of properties for common 3D printing materials are reported as a function of the dose. The performed multi-scale investigations include thermal, mechanical, and spectroscopic analyses, aiming at finding correlations between structural and macroscopic radiation effects.

3.2 Experimental Investigation on Polymers for 3D Printing

Polymeric materials for 3D printing are of increasing interest for the realization of components operating in extreme radiation conditions, not only in the medical field [43–45], but also for applications in particle accelerators, nuclear facilities [53, 54], and space missions [55, 56].

The existing literature on radiation effects in these materials primarily focuses on printed samples. However, the effects on the raw material, i.e. the printing filament, rather than the printed samples, must be thoroughly assessed, since the raw material reflects and generalizes the key consequences of irradiation on the printed item. Therefore, in the aim of this PhD project, a new research activity has been developed to broaden the available knowledge about radiation effects on popular 3D printing materials used for fused filament fabrication (FFF), namely the poly(lactic acid) (PLA), the acrylonitrile butadiene styrene (ABS), and a thermoplastic elastomer (TPE).

3.2.1 Sample Irradiation

The irradiations were conducted at the Hubert Curien Laboratory (LabHC) in Saint-Etienne, France, utilizing commercial X-ray tubes operating at a voltage of 160 kV, as shown in Figure 3.2a. Samples were placed on the supporting metal plate, and X-rays were emitted from the X-ray tube above. Printing filaments used as samples have a nominal diameter of 1.75 mm and a length of 10 cm in case the samples were used for tensile tests and 3 cm for the other analyses. The dose rate on the surface of the metal plate of support of samples was characterized using a PTW 23344 compact ionization chamber to guarantee that samples were exposed to a dose rate of 0.60 Gy/s (2.16 kGy/h) $\pm$ 15%, ensuring therefore a proper dose homogeneity in the irradiation area. In addition, such a low dose rate does not lead to significant heating of the sample. The various doses delivered to the samples are reported in Table 3.2, and the range goes from 45 kGy[H₂O] to 2 MGy[H₂O] (all the reported dose values refer to dose to water).

The energy spectrum of X-rays emitted by the tube depends on the material of the target in the X-ray tube, which in this case is tungsten, the anode angle (30°), and the inherent filtration, i.e. the layer of material used as the exit window of the X-ray beam (4 mm of beryllium). Based on these parameters, it is possible to estimate the spectrum (even after the filtration) by using

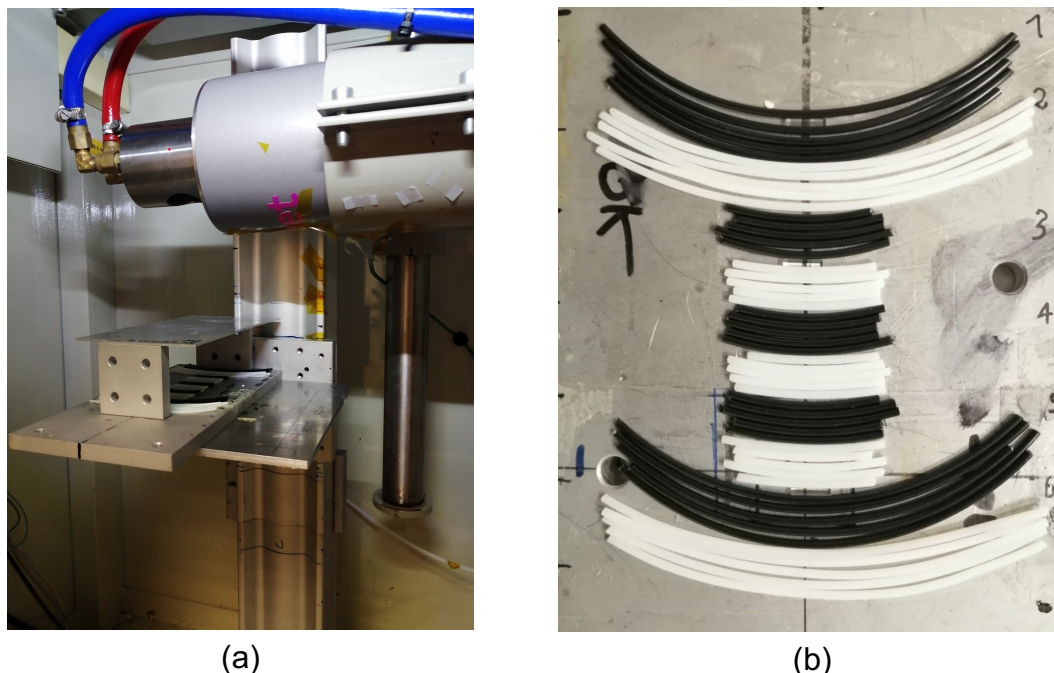


Figure 3.2: a) Irradiation setup, b) Printing filaments in ABS (black) and PLA (white) [46].

SpekPy v2.0 [57], and it is shown in Figure 3.3a. As expected, the maximum energy of X-ray photons is 160 keV, and most of the fluence is at relatively low energy (< 30 keV) and in correspondence with the characteristic peaks of tungsten. The low energy component is, however, not desirable, since such photons deposit most of the energy in the first millimeter of samples, leading to a non-negligible dose inhomogeneity in depth. For this reason, in the experimental setup, samples are placed below an aluminium foil 1.5 mm thick: this filter strongly attenuates photons up to (approximately) 30 keV, as shown in Figure 3.3a. On the other hand, the dose rate on the sample is reduced by almost a factor of ten by applying the aluminium filter, as reported in Figure 3.3b. Monte Carlo simulations performed by PHITS [58] were used to estimate the dose profiles. The dose was computed in 15 slices of a 1.75 mm diameter and 30 mm length cylinder of water exposed to an isotropic source of X-rays with an energy spectrum as the ones shown in Figure 3.3a.

The three printing materials investigated in this study are: PLA (Raise3D Premium, Irvine, CA, USA), ABS (Raise3D Premium ABS, Irvine, CA, USA), and TPE (Bioflex produced by Filoalfa and purchased by Maip Compounding S.r.l., Torino, Italy). PLA is a semi-crystalline polymer that is widely used because it is a biodegradable material and has low distortion during printing, despite being characterized by low thermal conductivity and mechan-

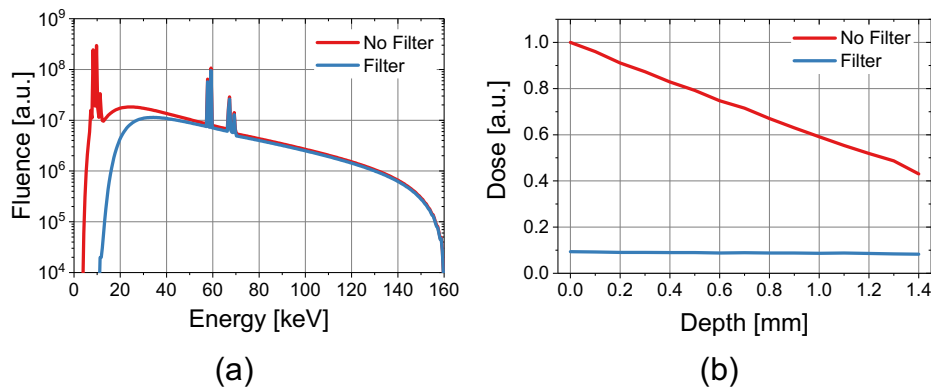


Figure 3.3: a) X-ray energy spectrum from SpekPy [57] and b) dose profiles in water estimated using PHITS, with and without a 1.5 mm thick aluminium filter [46].

ical properties [59]. ABS is instead an amorphous material [60] and it is not a biodegradable material. However, it is one of the most used printing materials because of its good mechanical properties and chemical properties [59]. Lastly, TPE is a thermoplastic elastomer composed of two distinct semicrystalline phases [61]. The material TPE is recyclable, and it has excellent chemical resistance as well as rubber-like elasticity [62].

The Hubert Curien Laboratory jointly with the Materials Science and Technology Laboratory (MaSTLab) of the University of Brescia (Italy) performed the sample characterization. More precisely, the performed multi-scale investigations include thermal, mechanical and spectroscopical analyses, more precisely the Thermogravimetric analysis (TGA), Differential scanning calorimetry (DSC), Dynamic Mechanical Thermal Analysis (DMTA), tensile test, Fourier transform infrared spectroscopy (FTIR), and Raman spectroscopy, aiming at finding correlations between structural and macroscopic radiation effects.

3.2.2 Tensile Test

The mechanical characteristics of samples (60 mm long) before and after irradiation were examined under tensile conditions at room temperature using an electromechanical dynamometer (model 3366, Instron, MA, US, crosshead speed of 50 mm/min). Tests were repeated on 5 samples for each material and each dose investigated, and from the nominal stress (σ) versus strain (ϵ) curves, it is possible to evaluate the Young's modulus (E) (i.e. the initial slope of the curves), the tensile strength (TS) (i.e. the maximum stress, which corresponds to the yield stress for specimens showing ductile failure

and to the ultimate stress for those showing brittle failure), and the strain at break (ϵ_b). In case specimens could not reach failure during the tests, as non-irradiated TPE, it is indicated that TS and ϵ_b are higher than the last recorded values.

A selection of stress-strain curves is reported in Figures 3.4, 3.5, 3.6, together with optical microscope images of the specimens. Young's modulus (E), tensile strength (TS), and strain at break (ϵ_b) of all the performed tests are reported in Table 3.2, showing the progressive radiation-induced damage on materials; in fact, at the highest doses all the materials become too brittle to be tested.

Among the investigated materials, the PLA shows the most significant deterioration in mechanical characteristics following irradiation. In pristine material, PLA stress-strain curves (Figure 3.4a) show a transition from an initial linear elastic response to a stress peak followed by a plateau, typical of ductile materials. In addition, Figures 3.4c and 3.4f show how the specimen's neck gradually thins until it breaks. However, even at the lowest dose (45 kGy) the specimens are severely embrittled, as shown by the stress-strain curves (Figure 3.4b) and the appearance of the samples after failure (see the absence of necking or other clear signs of yielding in Figures 3.4d and 3.4f). Table 3.2 shows that E and TS are lowered by 15-20% compared to non-irradiated values, whereas ϵ_b is reduced by about one order of magnitude. When the dosage is raised to 144 kGy (see Figures 3.4e and 3.4f), the material embrittlement is so strong that the specimens shatter during clamping.

The mechanical properties of the ABS filament don't vary much for doses up to 300 kGy, but a significant degradation is observed at doses of 1–2 MGy. The stress-strain curves for the samples that were irradiated at 292 kGy (Figure 3.5b) are similar to those for the unirradiated material (Figure 3.5a). They show ductile behavior with a linear elastic region up to the yield stress peak, then a strain-softening region, and finally a plateau. The broken specimens exhibit many white marks that are perpendicular to the load direction (Figure 3.5g), which are likely caused by yielding events. The more ductile the behavior, the more these white marks spread across the whole cross-section of the specimens. Indeed, the fractured surface of non-irradiated ABS has completely changed color (Figure 3.5d), while the fractured surface of ABS irradiated with 292 kGy (Figure 3.5e) is only partially white. On the other hand, at a dose of about 1 MGy (992 kGy, see Figure 3.5c, 3.5f, 3.5g), the

Filament	Dose [kGy]	E [MPa]	TS [MPa]	ϵ_b [%]
PLA	0	1960 $\pm$ 160	53.2 $\pm$ 0.6	33 $\pm$ 16
	45	1580 $\pm$ 200	45.5 $\pm$ 0.4	4.5 $\pm$ 0.3
	144	n.a. (too brittle to be tested)		
ABS	0	1470 $\pm$ 100	46.0 $\pm$ 0.2	31 $\pm$ 10
	45	1560 $\pm$ 90	43.5 $\pm$ 0.5	24 $\pm$ 4
	100	1620 $\pm$ 190	43.6 $\pm$ 1.1	12 $\pm$ 7
	139	1460 $\pm$ 200	43.7 $\pm$ 0.8	32 $\pm$ 10
	168	1520 $\pm$ 50	47.1 $\pm$ 0.3	26 $\pm$ 9
	251	1680 $\pm$ 50	47.6 $\pm$ 0.7	15 $\pm$ 3
	292	1470 $\pm$ 180	44.8 $\pm$ 0.2	21 $\pm$ 9
	992	1630 $\pm$ 250	30.1 $\pm$ 8.2	2 $\pm$ 1
	1900	n.a. (too brittle to be tested)		
TPE	0	33.3 $\pm$ 1.4	>12*	>800*
	45	31.9 $\pm$ 1.6	>12*	>800*
	100	32.6 $\pm$ 1.4	>12*	>800*
	139	29.3 $\pm$ 0.6	>12*	>800*
	168	33.1 $\pm$ 1.0	>12*	>800*
	251	30.8 $\pm$ 1.0	6.4 $\pm$ 0.3	250 $\pm$ 50
	292	27.8 $\pm$ 0.7	4.0 $\pm$ 0.1	43 $\pm$ 3
	910	n.a. (too brittle to be tested)		
	992	20.8 $\pm$ 0.3	2.2 $\pm$ 0.1	35 $\pm$ 3

* failure could not be reached

Table 3.2: Mechanical properties under tension for PLA, ABS, and TPE filaments tested in their pristine condition and after irradiation with various dose values: Young's modulus (E), tensile strength (TS), and strain at break (ϵ_b) [46].

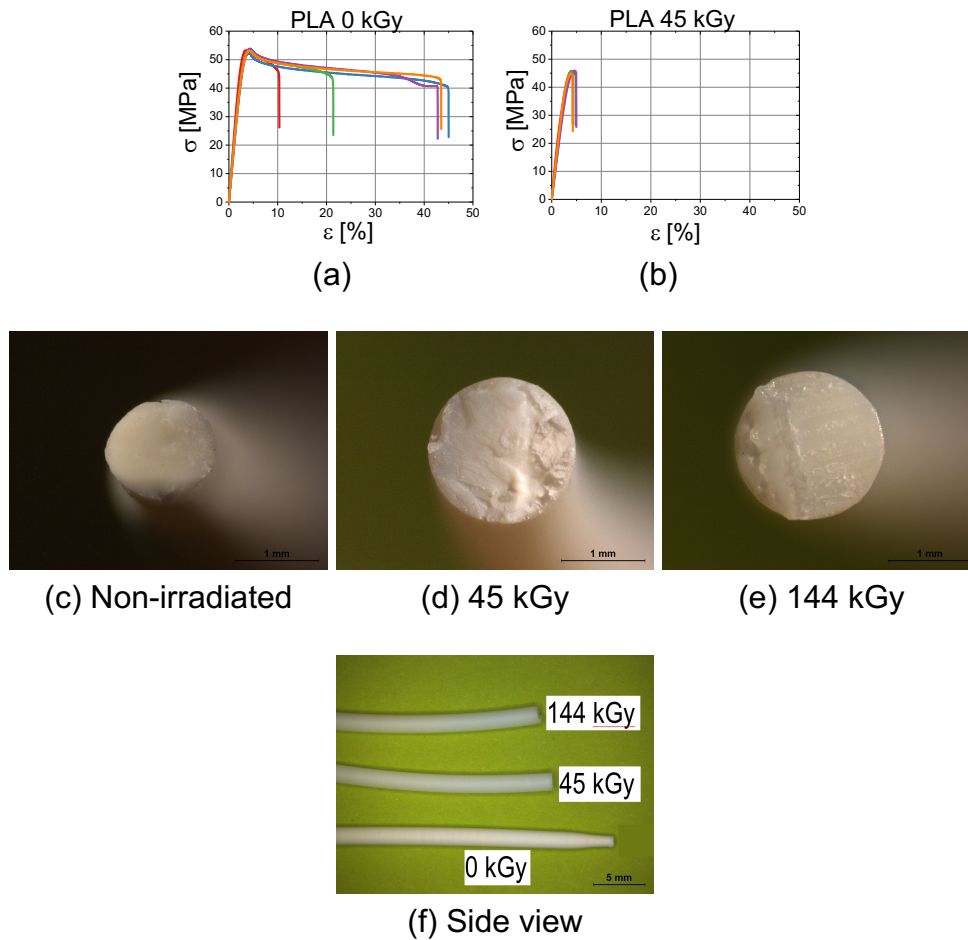


Figure 3.4: Tensile test results for PLA filaments tested in their pristine condition and after irradiation with different dose values, selected so to highlight the progressive embrittlement induced by X-rays: (a-b) stress-strain curves (each curve corresponds to one of the five samples exposed to the same dose); (c-f) optical microscope images of the specimens after the tests. Tensile test on the samples irradiated at 144 kGy was not possible [46].

ABS filament becomes much less ductile and shows stress-strain curves that are typical of brittle materials and no signs of yielding (see Figure 3.5c). Finally, ABS becomes so brittle at a dose of 1900 kGy that the specimens can't be tested because they were damaged when clamped in the tensile stress machine.

In order to better quantify the described effects, it is useful to compare the values of E , TS , and ϵ_b in Table 3.2. Irradiation up to 300 kGy makes no substantial changes to the characteristics of the pristine filament. Despite a minor drop in ϵ_b , the results remain comparable due to the high standard deviation. At a greater dosage of 1 MGy, TS is lowered by roughly one-third and ϵ_b by almost one order of magnitude compared to the comparable

beginning values, although E remains constant.

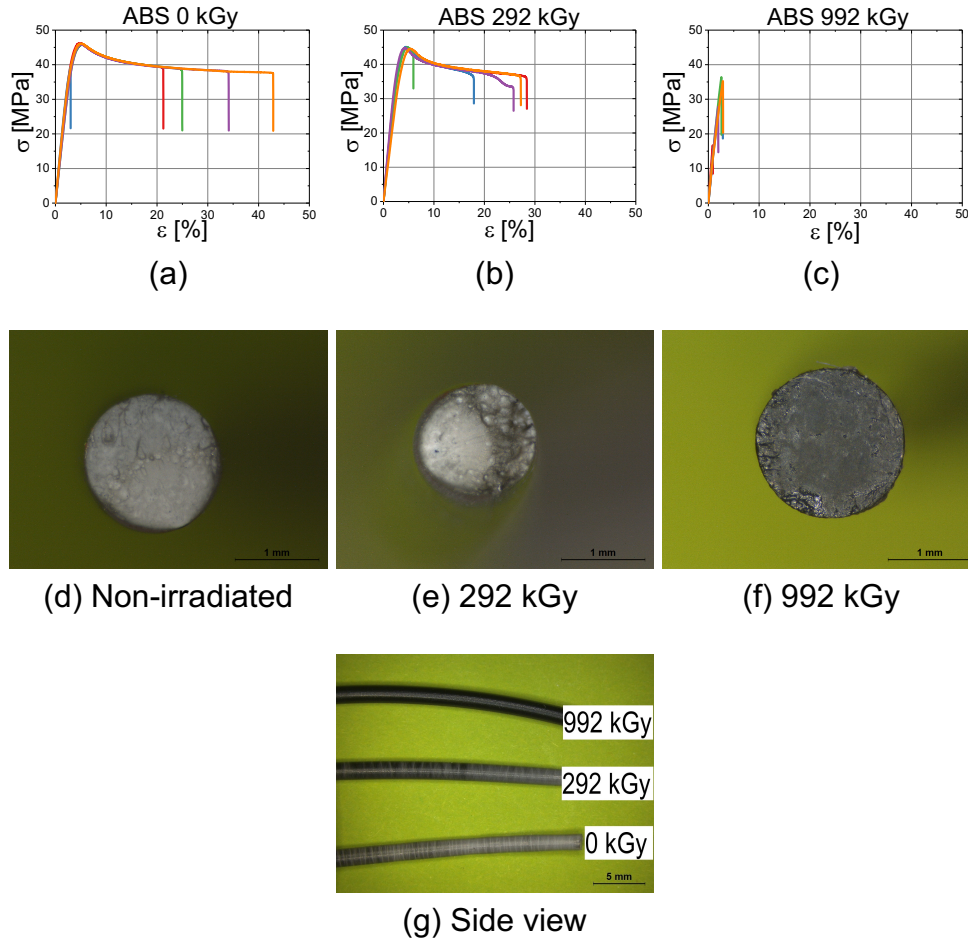


Figure 3.5: Tensile test results for ABS filaments tested in their pristine condition and after irradiation with different dose values, selected so to highlight the progressive embrittlement induced by X-rays: (a-c) stress-strain curves (each curve corresponds to one of the five samples exposed to the same dose); (d-g) optical microscope images of the specimens after the tests [46].

The impact of X-rays on the mechanical characteristics of the TPE filament becomes evident at dose levels of 250 kGy and above. It is significant that, at lower dose levels, the TPE may undergo deformation at strain values over 800% without fracturing; more than this value, the test could not proceed at further strain levels due to challenges in maintaining proper specimen grip.

The stress-strain curves exhibit nonlinear elastic behaviour, characterised by an initial zone with a steeper slope, followed by a knee that indicates the transition to a subsequent region with a lower slope (Figure 3.6a). The specimen's surface exhibits a smooth texture both before to and during the testing (Figure 3.6d). At dosages of around 250-300 kGy, the curves exhibit a comparable trend (Figure 3.6b); however, the specimens ultimately fail, with

fractures seeming to originate from the surface. Some of these cracks can be identified on the surface of the examined specimens (Figure 3.6f), although no cracks are observable under the optical microscope post-irradiation prior to the tensile test (refer to Figure 3.6e). In contrast, specimens subjected to a dose of approximately 1 MGy have a discernible repeating pattern of cracks post-irradiation but prior to testing (refer to Figure 3.6g), and they fracture at much reduced levels of stress and strain (Figure 3.6c). Additionally, a less shiny outer region may be identified in the cross-sections of the specimens that failed, suggesting the crack initiation site (Figure 3.6i). The appearance of pores and fissures on irradiated elastomers has been documented for certain rubbers subjected to high doses [63]; however, the distinctive pattern observed here is theoretically attributed to the combined effects of irradiation and residual stresses accrued during filament production.

Additional information on the evolution of TPE stiffness, strength, and ductility is shown in Table 3.2. No substantial changes in E are detected for dose levels up to at least 250 kGy, and the stiffness reduction reported at higher doses is likely to be attributable to the remarkable alteration in the specimen shape when cracks are clearly visible. On the other hand, a gradual drop in TS and ϵ_b is readily visible as more dose is absorbed. Specimens irradiated with dose levels below 200 kGy attain stress values surpassing 12 MPa and strain values over 800%, but at a dose of 250 kGy, TS falls below 6 MPa and ϵ_b below 250%. At larger dose additional damage is recorded, until, at levels approaching 1 MGy, specimens may become too brittle to be analysed. The specimens irradiated with 910 kGy and 992 kGy exhibited significant embrittlement, with only the latter being testable (TS $\approx$ 2 MPa; $\epsilon_b \approx$ 35%).

3.2.3 Thermal Tests

Both non-irradiated and irradiated specimens underwent a comprehensive series of thermal and thermo-mechanical tests, including Differential Scanning Calorimetry (DSC), Thermogravimetric Analysis (TGA), and Dynamic Mechanical Thermal Analysis (DMTA).

DSC measurements were performed using a DSC Q100 calorimeter (TA Instruments, New Castle, DE, USA) under a nitrogen atmosphere (50 mL/min). Approximately 10 mg samples, taken from both pristine and irradiated filaments, were subjected to the following thermal cycle: (i) heating from -80 °C to 280 °C at a rate of 10 °C/min; (ii) cooling from 128 °C to -80 °C at the

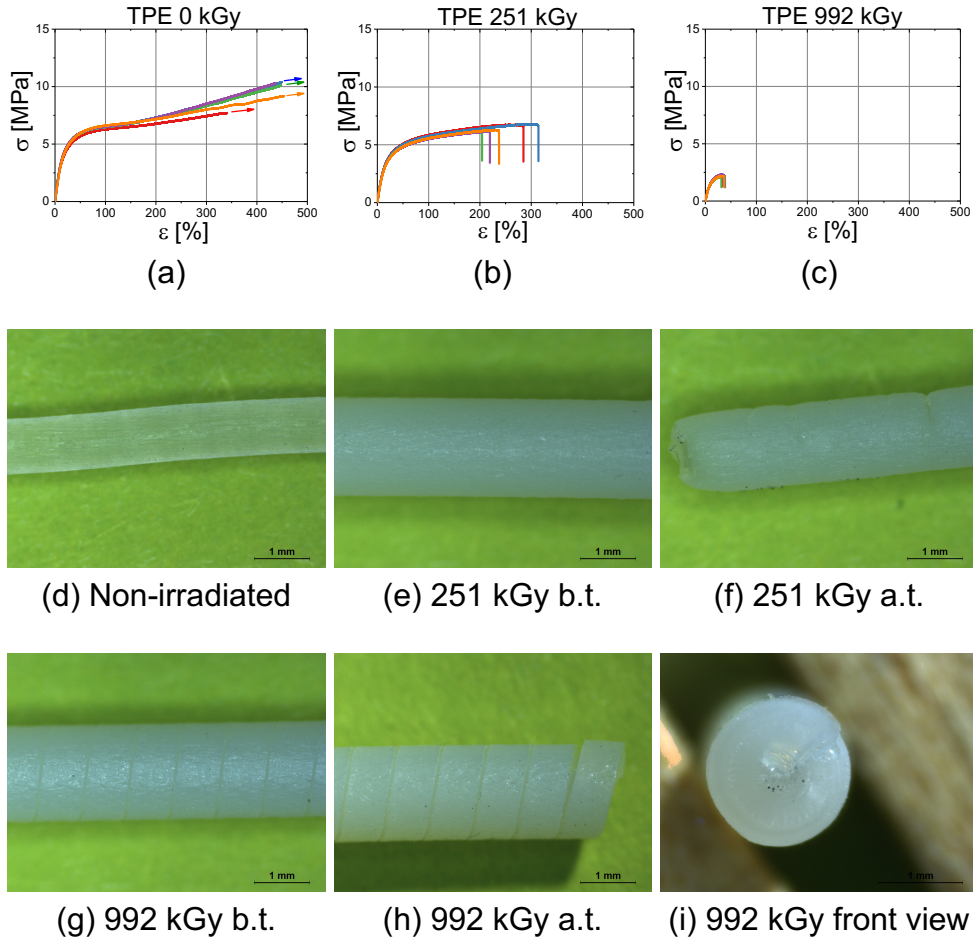


Figure 3.6: Tensile test results for TPE filaments tested in their pristine condition and after irradiation with different dose values, selected so to highlight the progressive embrittlement induced by X-rays (each curve corresponds to one of the five samples exposed to the same dose): (a-c) stress-strain curves; (d-g) optical microscope images of the specimens before and after the tests (b.t. and a.t.) [46].

same rate; (iii) reheating from $-80\text{ }^{\circ}\text{C}$ to $280\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C}/\text{min}$.

TGA analyses were carried out with a TGA Q500 analyser (TA Instruments, New Castle, DE, USA) on similarly sized ($\approx 10\text{ mg}$) samples from pristine and irradiated filaments. A continuous heating ramp from room temperature to $700\text{ }^{\circ}\text{C}$ at $10\text{ }^{\circ}\text{C}/\text{min}$ was applied.

DMTA testing was conducted using a DMA Q800 analyser (TA Instruments, New Castle, DE, USA). Small rods ($\approx 30\text{ mm}$ total length, $\approx 15\text{ mm}$ gauge length) were cut from the filaments for analysis in both pristine and irradiated states. However, irradiated PLA samples could not be tested due to embrittlement that caused consistent breakage during sample mounting. ABS and TPE specimens were analysed in dynamic tensile mode, using a

displacement amplitude of 15 μm and a frequency of 1 Hz. Heating was applied at a rate of 3 $^{\circ}\text{C}/\text{min}$ across temperature ranges specific to each polymer. Starting temperatures were chosen to ensure the analyses began below each material's glass transition point: room temperature for ABS and -40°C for TPE. Tests concluded when samples exceeded the analyser's elongation limit, typically during the onset of the flow regime at elevated temperatures.

To provide a comprehensive understanding of irradiation-induced material effects, the thermal characterisation was aimed at identifying alterations in thermal and mechanical behaviour. DSC was used to detect changes in thermal transitions (glass transition temperature T_g , melting temperature T_m , and cold crystallisation temperature T_{cc}) and in melting enthalpy (ΔH_m). TGA assessed shifts in the thermal degradation profile, focusing on the onset (T_{onset}) and peak (T_{peak}) degradation temperatures. DMTA evaluated the evolution of mechanical properties across temperature, including modifications in T_g and behaviour in the glassy, transition, rubbery, and early flow regimes.

Results of DSC and TGA analyses for PLA are shown in Figs. 3.7a and 3.7b, respectively. Despite pronounced embrittlement in PLA following irradiation, thermal analyses reveal only limited changes in these semicrystalline systems. The DSC results, presented as second heating scans, show that non-irradiated and moderately irradiated (45 kGy) specimens display similar thermal behaviour—initial recrystallisation followed by melting—with comparable T_g , T_{cc} , and T_m values (T_m measured at the highest endothermic peak), as listed in Table 3.3. Only the specimen subjected to the highest irradiation dose (144 kGy) exhibited significant differences: a reduction in T_g by nearly 20 $^{\circ}\text{C}$ and in T_m by approximately 10 $^{\circ}\text{C}$, a slight decrease in crystallinity (as indicated by the lower ΔH_m), and the absence of a cold crystallisation peak. TGA results showed a minor dose-dependent decrease in degradation onset temperature (T_{onset} , Table 3.3), while the overall degradation pathway and T_{peak} remained largely unaffected.

DSC and TGA analyses offer limited insight into the structural evolution of ABS, as shown in Figs. 3.8a and 3.8b, respectively. The DSC profiles, characteristic of an amorphous polymer, show negligible variation across all conditions, with the glass transition temperature remaining essentially unaffected by irradiation (Table 3.4). Similar to the findings for PLA, the TGA curves suggest that the overall degradation behaviour of ABS is largely pre-

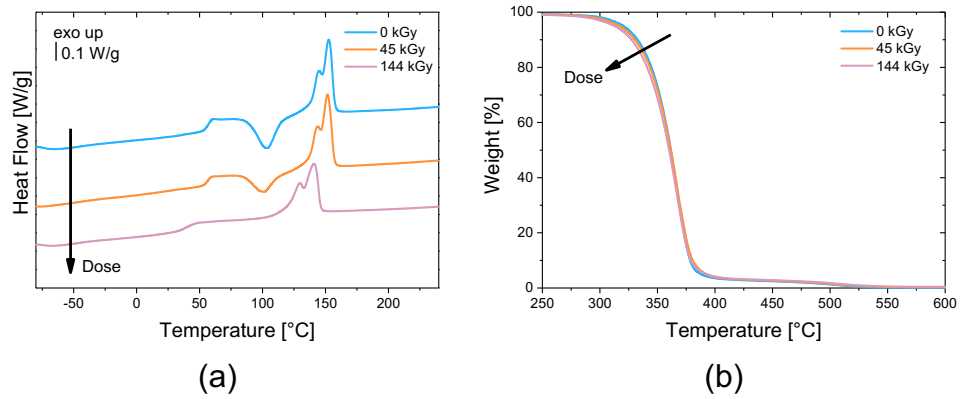


Figure 3.7: a) DSC traces (second heating scan) and b) TGA traces of PLA specimens, non-irradiated and subjected to various X-ray doses [46].

Dose [kGy]	DSC (2 nd heating scan)				TGA	
	T_g [°C]	T_{cc} [°C]	T_m [°C]	ΔH_m [J/g]	T_{onset} [°C]	T_{peak} [°C]
0	57.4	104	152.7	28.51	309.8	366.9
45	56.4	101.4	151.5	27.79	305.6	366.9
144	39.4	-	141	26.67	300	366.4

Table 3.3: Effect of the irradiation condition on DSC results (from second heating scan) and TGA results for variously irradiated PLA specimens [46].

served following irradiation. No significant changes are detected for doses up to 300 kGy. However, a slight reduction in both the onset and peak degradation temperatures is observed in the most heavily irradiated specimens (990 kGy and 1990 kGy), with the extent of the decrease becoming more evident at higher doses (see Table 3.4).

The storage modulus curves of ABS filaments, obtained via DMTA and shown in Fig. 3.8c, capture the full progression of the material's mechanical response as temperature increases. The curves illustrate the typical transition from high modulus values in the glassy region, through the glass transition zone, into the rubbery plateau, and finally into the flow regime—marked by a noticeable downward trend in the storage modulus. The transition from the glassy to the rubbery state appears consistent across all samples, reinforcing the DSC results which suggest minimal structural change due to irradiation. However, irradiation notably affects the terminal segment of the curves: as the absorbed dose increases, the onset of the flow regime shifts to progressively lower temperatures. This transition temperature, denoted

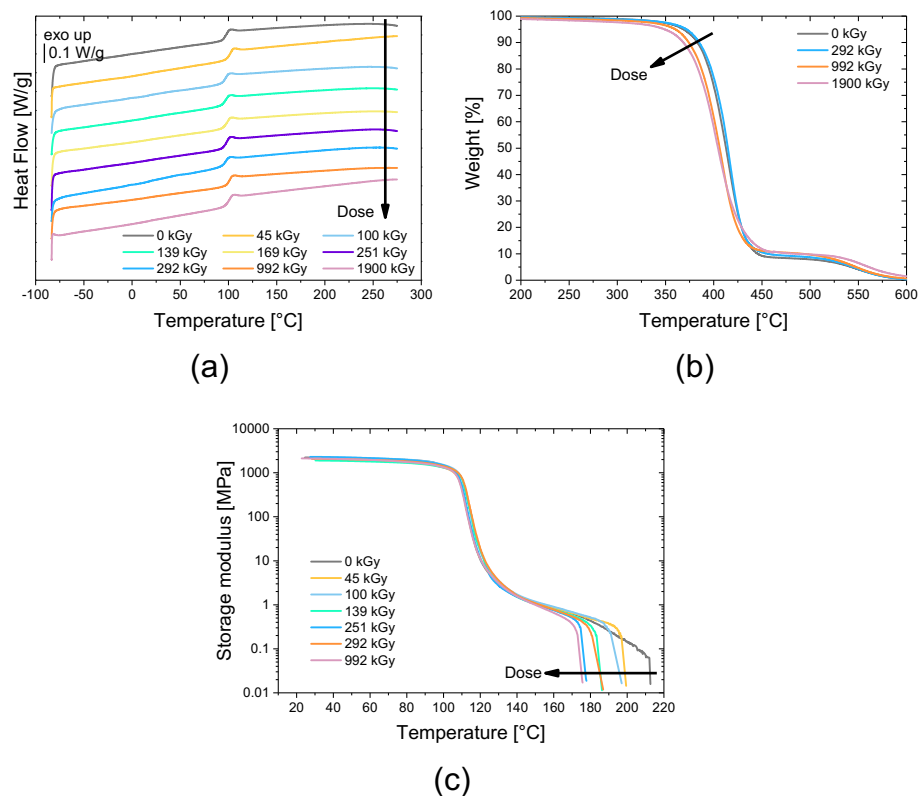


Figure 3.8: a) DSC traces (2nd heating scan), b) TGA traces, and c) DMTA storage modulus traces for ABS specimens, non-irradiated and subjected to various X-ray doses [46].

	DSC (2 nd heating scan)	TGA		DMTA
Dose [kGy]	T_g [°C]	T_{onset} [°C]	T_{peak} [°C]	T_{flow} [°C]
0	97.5	354.6	415.4	205
45	102.1	359.1	417.8	195
100	98.7	353.7	413.7	190
139	97.9	349.3	411.8	181
168	99.3	354.2	413.8	179
251	98.8	350.8	414.6	173
292	97.6	357.4	416.9	179
992	101.7	343.7	409.3	171
1900	101.6	324.2	403.2	-*

Table 3.4: Effect of the irradiation condition on DSC (from second heating scan), TGA and DMTA results for non-irradiated and variously irradiated ABS specimens (*: could not be tested due to severe embrittlement) [46].

as T_{flow} in Table 3.4, decreases gradually with increasing dose, showing a reduction of over 30 °C for doses approaching 1 MGy. At the highest irradiation level (≈ 2 MGy), extensive embrittlement prevented mechanical testing of the specimens

In the case of TPE, DSC analysis reveals a distinct exothermal anomaly during the first heating scan (Fig. 3.9a), which disappears in the second scan (Fig. 3.9b). The latter shows only two endothermic peaks corresponding to the melting of the soft (low-temperature) and hard (high-temperature) domains. These peaks align with those previously reported in literature for Bioflex® [61], attributed to the melting of soft and hard segments in a thermoplastic copolyester-ether elastomer. In the first heating scan of irradiated samples, the exothermal signal becomes more pronounced and shifts to lower temperatures as radiation dose increases, as reflected in the peak temperature (T_{exo}) and enthalpy (ΔH_{exo}) values listed in Table 3.5. At intermediate doses (100 kGy and 140 kGy), the ΔH_{exo} values are less significant due to overlap with the hard segment melting peak. This exothermic anomaly likely indicates early degradation, corroborated by TGA results (Fig. 3.9c), which show a dose-dependent decrease in the onset temperature of thermal degradation (T_{onset} in Table 3.5) by 10 °C at 45 kGy and up to 80 °C at 992 kGy.

In contrast, the second heating scan reveals no significant changes with increasing dose: both melting temperatures (T_{m1} and T_{m2} , for the soft and hard domains respectively) and their corresponding enthalpies (ΔH_{m1} and ΔH_{m2}) remain largely unaffected, except in the most heavily irradiated samples (910 kGy and 990 kGy). These specimens exhibit a slight decrease in ΔH_{m1} , suggesting reduced crystallinity in the soft domain, and a 20 °C reduction in T_{m2} , indicating the formation of lower-quality hard domain crystals (Table 3.5).

DMTA results reveal a consistent mechanical response across all TPE samples. Initially, the storage modulus gradually decreases from –50 °C to 0 °C, attributed to the melting of the soft crystalline phase, followed by an extended, gently sloped plateau. Eventually, the modulus declines sharply, marking the onset of the flow regime as the hard domains begin to melt. The temperature at which this deviation occurs, defined as T_{flow} in Table 3.5, decreases progressively with increasing radiation dose.

Based on the influence of irradiation, TPE specimens can be grouped into three categories:

- Low-dose group (≤ 100 kGy): Storage modulus curves and flow transition temperatures remain unaffected by irradiation.
- Intermediate-dose group (100–300 kGy): The onset of the flow regime is modestly reduced, by no more than 10 °C.
- High-dose group (≥ 910 kGy): A pronounced reduction in T_{flow} is observed—by 20 °C for 990 kGy and 30 °C for 910 kGy. Additionally, the storage modulus at fixed temperatures is lower, consistent with a decrease in Young's modulus measured via tensile testing at room temperature.

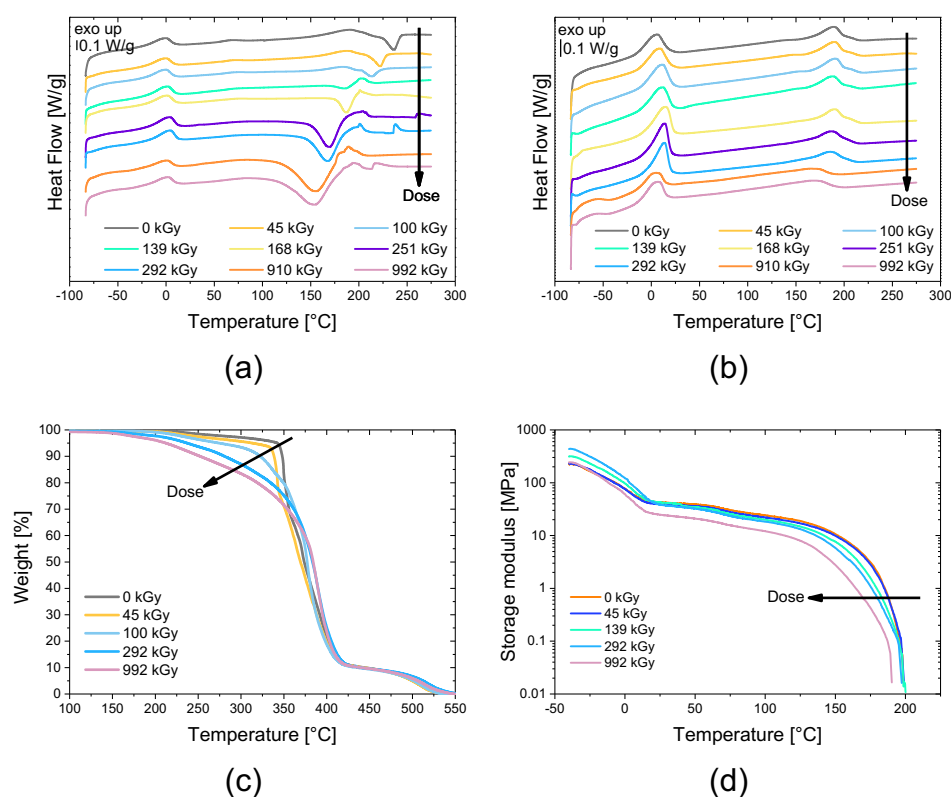


Figure 3.9: DSC traces (a) first and b) second heating scan), c) TGA traces, and d) DMTA storage modulus traces for TPE specimens, non-irradiated and subjected to various X-ray doses [46].

3.2.4 Spectroscopy Tests

FTIR analysis was carried out using a Thermo Scientific Nicolet iS50 FTIR spectrophotometer (Thermo Fisher Scientific, Madison, WI, US) equipped with a PIKE MIRacle attenuated total reflectance (ATR) accessory. Spectra were collected in the range of 600–4000 cm^{-1} . Raman spectroscopy was

3.2. EXPERIMENTAL INVESTIGATION ON POLYMERS FOR 3D PRINTING

	DSC						TGA		DMTA
	1 st heating scan		2 nd heating scan						
Dose [kGy]	T _{exo} [°C]	ΔH _{exo} [J/g]	T _{m1} [°C]	ΔH _{m1} [J/g]	T _{m2} [°C]	ΔH _{m2} [J/g]	T _{onset} [°C]	T _{peak} [°C]	T _{flow} [°C]
0	236.5	13.3	5.7	18.6	189.3	11.9	212.2	350.9	159
45	222.3	10.5	8.5	16.7	189.9	11.3	200.2	341.4	159
100	213.9	5.3	11.2	18.7	191	10.6	177.4	378.4	158
139	185.5	4.9	11	18.8	188.6	9.9	167.5	367.7	154
168	187.4	12.1	14.5	22.4	190.4	13.4	163.7	359.1	152
251	169.7	40.2	13.7	23.2	186.8	14.3	152.3	374.2	151
292	168.3	46.7	13.4	20.6	185.8	12.6	147.4	389.9	150
910	155.9	71.2	2.9	12.5	164.6	8.3	143.1	388.5	128
992	154.5	70.7	5.2	16.5	167.7	11.2	123.1	390.2	139

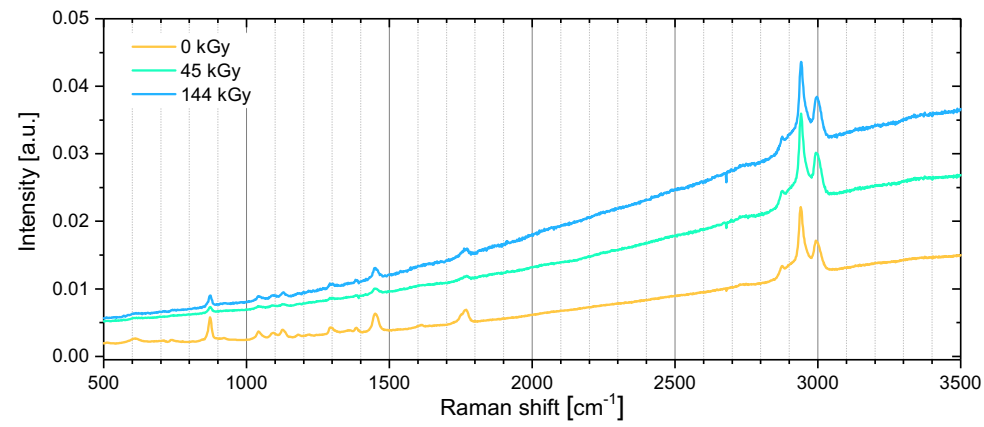
Table 3.5: Effect of the irradiation condition on DSC (from first and second heating scans), TGA and DMTA results for non-irradiated and variously irradiated TPE specimens [46].

performed using an inVia Qontor Raman microscope (Renishaw plc, UK) with a laser excitation wavelength of 442 nm. Raman spectra were recorded across the 500–3500 cm⁻¹ range. For Raman measurements, samples were sectioned perpendicular to the filament axis, and data were collected at three radial locations on the cut surface: near the outer surface, near the core, and at an intermediate point.

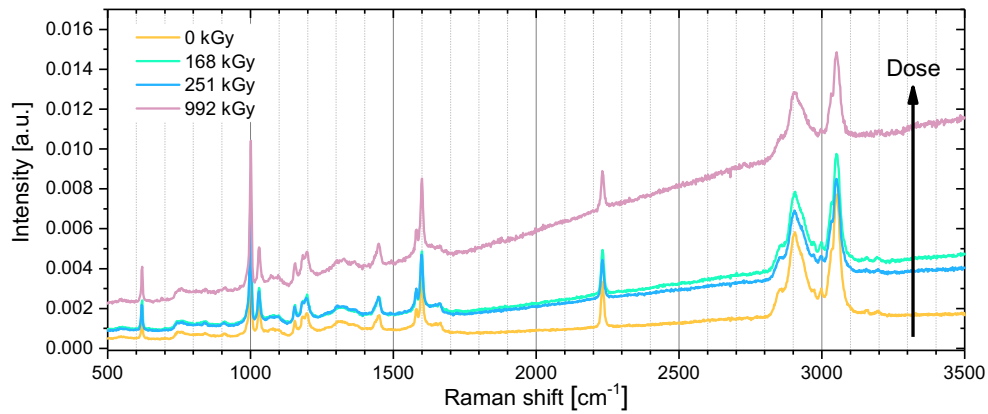
The FTIR spectra of non-irradiated filaments were found to be broadly consistent with literature reports [61, 64, 65]. Upon irradiation, all materials exhibited spectral features indicative of oxidation, most notably the appearance of a broad absorption band in the 3100–3600 cm⁻¹ region, attributed to O–H stretching vibrations. Aside from this oxidation signal, the remainder of the spectra showed no significant shifts in peak positions and only minor variations in intensity, suggesting limited changes in the overall chemical structure of the filaments.

Raman spectra acquired from the three materials were also consistent with previous literature data [61, 64, 66]. All spectra were normalized to the total Raman peak area and are presented as a function of irradiation dose in Figure 3.10.

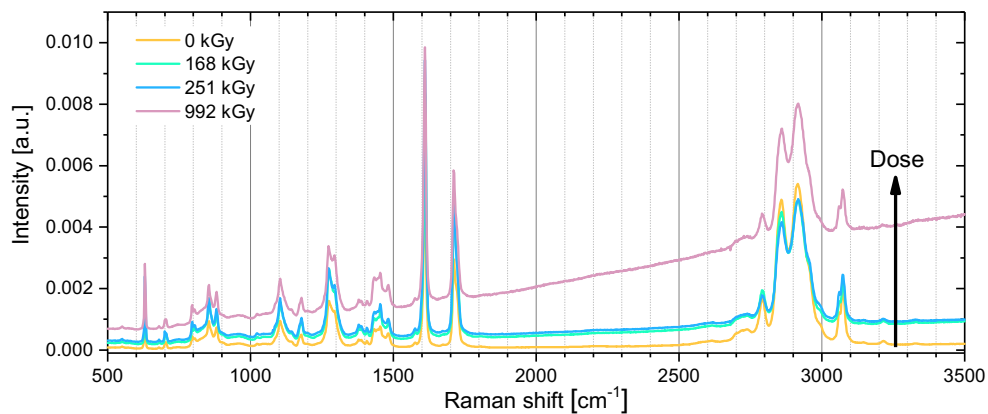
For both ABS and TPE, the Raman spectra did not show significant changes in peak positions or relative intensities as a function of irradiation dose. However, an increase in the fluorescence background was observed with increasing absorbed dose. In the case of ABS, a slight broadening of the peak at 1600 cm⁻¹—associated with the skeletal vibration of the C=C aromatic ring [66]—was also noted.



(a)



(b)



(c)

Figure 3.10: Raman normalized spectra for a) PLA, b) ABS and c) TPE filaments [46].

No substantial differences were detected in ABS spectra based on the sampling position along the filament radius. In contrast, for TPE irradiated at high doses, a systematic increase in fluorescence background was observed across the filament cross-section, with higher background levels consistently recorded near the outer surface, as illustrated in Figure 3.11.

Regarding PLA, the Raman spectra exhibited low repeatability in terms of fluorescence background intensity. Nonetheless, no new spectral features emerged across the different irradiation conditions.

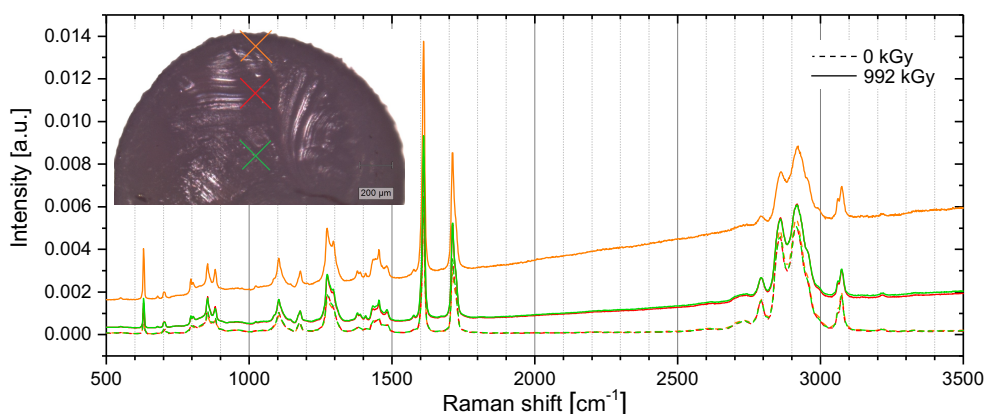


Figure 3.11: Raman spectra for non-irradiated (dotted lines) and irradiated (at 992 kGy, solid lines) TPE filament in function of the position along the radius of the filament [46].

3.2.5 Analysis and Results

The marked deterioration in mechanical properties, in contrast to the relatively modest changes in chemical and thermal characteristics, supports the hypothesis that chain scission is the dominant radiation-induced mechanism affecting all three materials examined, as discussed below.

In the case of PLA, mechanical properties degrade significantly with increasing X-ray dose. While non-irradiated specimens exhibit ductile behaviour and undergo substantial plastic deformation, even the lowest investigated dose (45 kGy) leads to brittle failure. At 144 kGy, degradation is so severe that specimens become untestable. These findings align with previous reports on gamma-irradiated PLA [65, 67]. For instance, West et al. [67] and Wady et al. [65] were able to test samples up to 150 kGy and 300 kGy, respectively; however, above 100 kGy, strain at break consistently dropped below 1%, and tensile strength decreased by more than 50%, indicating severe

embrittlement. The slight discrepancy in dose thresholds for tensile testing compared to the present study may stem from differences in experimental conditions, such as radiation type, dose rate, strain rate, or sample geometry.

Thermal analysis via DSC provides subtle but meaningful insights into the effects of radiation on PLA. The observed decrease in glass transition temperature (T_g) and melting temperature (T_m), the slight reduction in melting enthalpy (ΔH_m), and the disappearance of the cold crystallisation peak in the most irradiated samples (144 kGy) are consistent with a reduction in molecular weight due to chain scission. The presence of shorter chains may contribute to a plasticising effect that lowers T_g , impairs the formation of well-ordered crystals (reflected in decreased T_m and ΔH_m), and facilitates more complete crystallisation upon cooling, eliminating the need for recrystallisation during the second heating scan. These trends mirror observations in studies on gamma-irradiated PLA [65, 67, 68]. Regarding melting enthalpy, similar reductions in ΔH_m have been reported for doses up to 150 kGy, while higher doses have been associated with an increase in crystallinity [68].

TGA results also indicate modest but relevant changes, consistent with literature on PLA exposed to gamma radiation from ^{60}Co sources up to 400 kGy [65, 67]. In those studies, higher doses correlated with an increased mass loss during the early stages of thermal degradation, attributed to chain scission and the formation of thermally labile peroxy groups that decompose upon heating [69]. Altogether, the observed deterioration in mechanical performance and the supporting thermal data reinforce the conclusion that chain scission is the predominant radiation-induced mechanism in PLA.

The tensile properties of ABS filament remain largely unaffected by irradiation doses up to 300 kGy. However, at higher doses between 1 and 2 MGy, substantial changes are observed. Tensile testing reveals a radiation-induced transition from ductile to brittle behaviour, marked by reductions in both tensile strength (TS) and elongation at break (ϵ_b), while the Young's modulus (E) remains unchanged. This trend aligns with previous findings on ABS exposed to gamma irradiation at doses below 1 MGy [55, 65]. At the highest dose tested (1900 kGy), samples become mechanically untestable.

Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA) provide limited insight into the structural evolution of ABS. The glass transition temperature (T_g) stays constant, although both the onset (T_{onset}) and peak (T_{peak}) degradation temperatures exhibit slight reductions

with increasing dose. This decline has also been reported in literature and is typically attributed to the enhanced volatilization of low molecular weight fragments formed during high-dose gamma irradiation (2.68 MGy) [65].

Dynamic Mechanical Thermal Analysis (DMTA) in this study shows a dose-dependent shortening of the rubbery plateau, indicating a progressive decrease in molecular weight due to X-ray exposure. The extent of the rubbery plateau generally correlates with polymer chain length: more precisely, shorter chains are less entangled, reducing this plateau and anticipating the onset of flow behaviour. This observation suggests that chain scission dominates over crosslinking in ABS irradiated with X-rays up to 1 MGy. This conclusion is further supported by the stable Young's modulus, which shows no signs of radiation-induced stiffening. In contrast, gamma irradiation has been linked to crosslinking at similar dose levels, as inferred from the increase in stiffness[65]. Nevertheless, the concurrent drop in tensile strength in gamma-irradiated ABS may still be attributable to chain scission. Given the overlapping mechanisms and varying dose ranges, current evidence does not definitively support a distinct effect of X-rays versus gamma rays on ABS.

Raman spectroscopy on ABS supports these findings: an increase in spectral background suggests radical-induced fluorescence, while broadening of the 1600 cm^{-1} band indicates the formation of additional carbonyl groups, consistent with previous reports [65].

The most pronounced radiation-induced mechanical degradation is observed in the TPE samples. Initially capable of sustaining elongations exceeding 800%, the material becomes extremely brittle at doses near 1 MGy. Above 250 kGy, tensile strength, elongation at break (ϵ_b), and Young's modulus all decline noticeably with increasing dose. DSC results suggest that the crystalline structure of TPE remains mostly unaffected until around 1 MGy, where slight reductions in soft domain crystallinity and the quality of hard domain crystals are detected. On the other hand, thermal stability is significantly compromised: both TGA and DSC reveal earlier onset of degradation with increasing dose. Additionally, DMTA results show that the flow transition temperature of TPE decreases progressively at doses above 100 kGy.

A notable observation is the progressive shift indicative of a reduction in molecular weight, likely due to chain scission processes. This interpretation is supported by the observed decline in mechanical properties such as strength and ductility. At higher radiation doses (around 1 MGy), a noticeable reduction in stiffness is also recorded, affecting both Young's modulus and

storage modulus. This may be attributed to the cracks which appeared on the surface of the filaments after irradiation at such high doses, significantly altering the specimens' geometry. Additionally, TPE exhibits an increased fluorescence background in the Raman spectra post-irradiation. This fluorescence enhancement is more prominent near the surface, suggesting potential oxygenation effects influenced by material porosity, geometry, and other factors, which affect radical formation and subsequent damage. This phenomenon correlates with the surface cracks observed on the TPE filaments irradiated at high doses. However, it remains unclear whether increased oxygenation is the cause or a consequence of the cracking, underscoring the need for further research to clarify the relationship between oxygen ingress and structural deterioration.

Overall, the irradiation results indicate a gradual degradation of material properties with increasing dose, predominantly affecting mechanical characteristics more than chemical or thermal ones. The data consistently support chain scission as the primary damage mechanism.

Sample geometry appears to play a significant role in the observed effects, as inferred from the spectroscopic behavior of TPE. Oxygenation contributes to more severe damage, suggesting that degradation in filament form may differ from that in 3D-printed objects. These differences stem from variations in oxygen diffusion dynamics, which are influenced by factors such as sample thickness, surface area, porosity, and overall geometry.

The findings also facilitate a comparative assessment of the materials' radiation tolerance, offering valuable insights for selecting the most resilient options. Among the three tested materials, PLA shows the lowest tolerance, with a marked drop in tensile strength beyond 100 kGy. In contrast, TPE and ABS demonstrate superior radiation resistance, showing comparable mechanical degradation only after 1 MGy and 2 MGy, respectively. Future experiments will further explore the influence of parameters such as temperature, ambient environment, sample geometry, and dose rate on radiation effects, particularly in relation to oxygenation. Preliminary results indicate no significant difference between samples irradiated at 0.2 Gy/s and 0.6 Gy/s, prompting further investigation using a substantially higher dose rate (via 2.5 MeV electron beam exceeding 10 MGy/h).

Conclusion

This thesis explores industrial sterilization using ionizing radiation, with a particular focus on electron beam (e-beam) sterilization.

Monte Carlo simulations were employed to accurately model dose distributions within real product geometries and packaging configurations. Specifically, simulations performed on commercial products provided deeper insights into electron interactions with the product boxes and enabled quantification of strategies to optimize dose distribution. These simulations also guide the estimation of optimal process parameters to minimize sterilization time without compromising process quality.

The effects of specific configuration choices—such as placing denser product components at the bottom of the box during single-side irradiation, and the use of scattering plates—were assessed. Both approaches were found to significantly reduce the Dose Uniformity Ratio (DUR). Furthermore, uncertainty quantification added confidence to the simulation outcomes, supporting systematic process optimization aimed at increasing throughput.

In addition, this thesis investigated the effects of ionizing radiation on several commercial polymers commonly used in Fused Filament Fabrication (FFF) 3D printing, which are gaining relevance also in the medical sector. Combined mechanical, thermal, and spectroscopic analyses revealed progressive material degradation with increasing radiation dose, primarily impacting mechanical properties more than chemical or thermal ones. Results consistently indicate chain scission as the dominant degradation mechanism. Among the three tested polymers, PLA exhibited the lowest radiation

tolerance, with a significant decrease in tensile strength beyond 100 kGy. In contrast, TPE and ABS showed higher resistance, with similar levels of mechanical degradation occurring only after exposure to 1 MGy and 2 MGy, respectively.

Overall, this work contributes to both the optimization of industrial e-beam sterilization processes and the broader understanding of polymer behavior under ionizing radiation. The proposed simulation framework supports more efficient process design while preserving product integrity. These findings offer practical value to Copan and similar manufacturers in selecting appropriate materials and irradiation strategies.

Bibliography

- [1] Angelo Nespoli, Stefanos Geroulanos, Armando Nardone, Sara Coppola, and Luca Nespoli.
The history of surgical infections.
Surgical Infections, 12(1):3–13, February 2011.
ISSN 1557-8674.
doi: 10.1089/sur.2010.106.
URL <http://dx.doi.org/10.1089/sur.2010.106>.
- [2] Mine Silindir Gunay and Yekta Ozer.
Sterilization methods and the comparison of e-beam sterilization with gamma radiation sterilization.
FABAD J Pharm Sci, 34:43–53, 01 2009.
- [3] Waldemar Scharf and Wioletta Wieszczycka.
Electron accelerators for industrial processing—a review.
In *AIP Conference Proceedings*, page 949–952. AIP, 1999.
doi: 10.1063/1.59300.
URL <http://dx.doi.org/10.1063/1.59300>.
- [4] Gisela C.C. Mendes, Teresa R.S. Brandão, and Cristina L.M. Silva.
Ethylene oxide sterilization of medical devices: A review.
American Journal of Infection Control, 35(9):574–581, November 2007.
ISSN 0196-6553.
doi: 10.1016/j.ajic.2006.10.014.
URL <http://dx.doi.org/10.1016/j.ajic.2006.10.014>.
- [5] W.A. Rutala and D.J. Weber.
Infection control: the role of disinfection and sterilization.
Journal of Hospital Infection, 43:S43–S55, December 1999.
ISSN 0195-6701.
doi: 10.1016/s0195-6701(99)90065-8.
URL [http://dx.doi.org/10.1016/s0195-6701\(99\)90065-8](http://dx.doi.org/10.1016/s0195-6701(99)90065-8).

- [6] U.S. Chemical Safety and Hazard Investigation Board.
Sterigenics ethylene oxide explosion.
<https://www.csb.gov/sterigenics-ethylene-oxide-explosion/>,
2006.
- [7] Glenn F Knoll.
Radiation detection and measurement; 4th ed.
Wiley, New York, NY, 2010.
URL <https://cds.cern.ch/record/1300754>.
- [8] Fred A Mettler.
Medical effects and risks of exposure to ionising radiation.
Journal of Radiological Protection, 32(1):N9–N13, March 2012.
ISSN 1361-6498.
doi: 10.1088/0952-4746/32/1/n9.
URL <http://dx.doi.org/10.1088/0952-4746/32/1/N9>.
- [9] Thomas K. Kroc.
Monte carlo simulations demonstrating physics of equivalency of
gamma, electron-beam, and x-ray for radiation sterilization.
Radiation Physics and Chemistry, 204:110702, March 2023.
ISSN 0969-806X.
doi: 10.1016/j.radphyschem.2022.110702.
URL <http://dx.doi.org/10.1016/j.radphyschem.2022.110702>.
- [10] Stephen Seltzer.
Tables of x-ray mass attenuation coefficients and mass energy-
absorption coefficients, nist standard reference database 126, 1995.
URL <http://www.nist.gov/pml/data/xraycoef/index.cfm>.
- [11] A.J. Koning, D. Rochman, J.-Ch. Sublet, N. Dzysiuk, M. Fleming, and
S. van der Marck.
Tendl: Complete nuclear data library for innovative nuclear science and
technology.
Nuclear Data Sheets, 155:1–55, January 2019.
ISSN 0090-3752.
doi: 10.1016/j.nds.2019.01.002.
URL <http://dx.doi.org/10.1016/j.nds.2019.01.002>.
- [12] Zbigniew Zimek.

- Economical evaluation of radiation processing with high-intensity x-rays.
Nukleonika, 65(3):167–172, July 2020.
ISSN 0029-5922.
doi: 10.2478/nuka-2020-0027.
URL <http://dx.doi.org/10.2478/nuka-2020-0027>.
- [13] Oswaldo Baffa and Angela Kinoshita.
Clinical applications of alanine/electron spin resonance dosimetry.
Radiation and Environmental Biophysics, 53(2):233–240, January 2014.
ISSN 1432-2099.
doi: 10.1007/s00411-013-0509-2.
URL <http://dx.doi.org/10.1007/s00411-013-0509-2>.
- [14] Marc F Desrosiers, Sarenée L Cooper, James M Puhl, Anna L McBain, and Glenn W Calvert.
A study of the alanine dosimeter irradiation temperature coefficient in the -77°C to $+50^{\circ}\text{C}$ range.
Radiation Physics and Chemistry, 71(1–2):365–370, September 2004.
ISSN 0969-806X.
doi: 10.1016/j.radphyschem.2004.04.066.
URL <http://dx.doi.org/10.1016/j.radphyschem.2004.04.066>.
- [15] Olga F Sleptchonok, Vitaly Nagy, and Marc F Desrosiers.
Advancements in accuracy of the alanine dosimetry system. part 1. the effects of environmental humidity.
Radiation Physics and Chemistry, 57(2):115–133, February 2000.
ISSN 0969-806X.
doi: 10.1016/S0969-806X(99)00338-2.
URL [http://dx.doi.org/10.1016/S0969-806X\(99\)00338-2](http://dx.doi.org/10.1016/S0969-806X(99)00338-2).
- [16] M. F. Desrosiers, J. M. Puhl, and S. L. Cooper.
An absorbed-dose/dose-rate dependence for the alanine-epr dosimetry system and its implications in high-dose ionizing radiation metrology.
Journal of Research of the National Institute of Standards and Technology, 113(2):79, March 2008.
ISSN 1044-677X.

doi: 10.6028/jres.113.007.

URL <http://dx.doi.org/10.6028/jres.113.007>.

- [17] Matthew Williams, Peter Metcalfe, Anatoly Rosenfeld, Tomas Kron, Francesco d'Errico, and Marko Moscovitch.

Radiochromic film dosimetry and its applications in radiotherapy.

In *AIP Conference Proceedings*, page 75–99. AIP, 2011.

doi: 10.1063/1.3576160.

URL <http://dx.doi.org/10.1063/1.3576160>.

- [18] Christopher Soares, Sameul Trichter, and Slobodan Devic.

Radiochromic Film.

2009 AAPM Summer School, AAPM, College Park, MD, 2009-12-31 2009.

URL https://tsapps.nist.gov/publication/get_pdf.cfm?pub_id=901164.

- [19] Luiz Carlos Duarte Ladeira, Amir Zacarias Mesquita, and Márcio Tadeu Pereira.

Calibrations of red perspex pmma dosimeter in terms of absorbed dose to water for routine dosimetry at cdtn gamma irradiation laboratory.

International Journal of Nuclear Energy Science and Technology, 9(3): 238, 2015.

ISSN 1741-637X.

doi: 10.1504/ijnest.2015.074099.

URL <http://dx.doi.org/10.1504/IJNEST.2015.074099>.

- [20] KM Glover, ME Plested, MF Watts, and B Whittaker.

A study of some parameters relevant to the response of harwell pmma dosimeters to gamma and electron irradiation.

Radiation Physics and Chemistry, 42(4–6):739–742, October 1993.

ISSN 0969-806X.

doi: 10.1016/0969-806x(93)90363-y.

URL [http://dx.doi.org/10.1016/0969-806X\(93\)90363-Y](http://dx.doi.org/10.1016/0969-806X(93)90363-Y).

- [21] Standard practice for use of a cellulose triacetate dosimetry system.

doi: 10.1520/isoastm51650-13.

URL <http://dx.doi.org/10.1520/ISOASTM51650-13>.

- [22] Copan.

<https://www.copangroup.com/>.

- [23] Jacques Pottier.
A new type of rf electron accelerator: The rhodotron.
Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms, 40–41:943–945, April 1989.
ISSN 0168-583X.
doi: 10.1016/0168-583x(89)90512-0.
URL [http://dx.doi.org/10.1016/0168-583X\(89\)90512-0](http://dx.doi.org/10.1016/0168-583X(89)90512-0).
- [24] J. M. Bassaler and H. Baudrand.
Boundary integral method applied to the rhodotron accelerator cavity.
Journal de Physique III, 3(3):573–580, March 1993.
ISSN 1286-4897.
doi: 10.1051/jp3:1993150.
URL <http://dx.doi.org/10.1051/jp3:1993150>.
- [25] Marshall R. Cleland.
Radio-frequency electron accelerators for industrial applications.
Reviews of Accelerator Science and Technology, 04(01):213–218, January 2011.
ISSN 1793-8058.
doi: 10.1142/s1793626811000537.
URL <http://dx.doi.org/10.1142/S1793626811000537>.
- [26] Yves Jongen.
Manufacturing of electron accelerators.
In *Proceedings of the European Particle Accelerator Conference*, pages 260–263, 1996.
- [27] Marc Van Lancker, Arnold Herer, Marshall R. Cleland, Yves Jongen, and Michel Abs.
The iba rhodotron: an industrial high-voltage high-powered electron beam accelerator for polymers radiation processing.
Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms, 151(1–4):242–246, May 1999.
ISSN 0168-583X.
doi: 10.1016/s0168-583x(99)00099-3.
URL [http://dx.doi.org/10.1016/S0168-583X\(99\)00099-3](http://dx.doi.org/10.1016/S0168-583X(99)00099-3).

- [28] Iraj Jabbari, Ali Mohammad Poursaleh, and Hossein Khalafi.
Design study of double-layer beam trajectory accelerator based on the
rhodotron structure.
*Nuclear Instruments and Methods in Physics Research Section A: Ac-
celerators, Spectrometers, Detectors and Associated Equipment*,
828:72–80, August 2016.
ISSN 0168-9002.
doi: 10.1016/j.nima.2016.04.112.
URL <http://dx.doi.org/10.1016/j.nima.2016.04.112>.
- [29] Y. Jongen, M. Abs, F. Genin, A. Nguyen, J.M. Capdevila, and D. Defrise.
The rhodotron, a new 10 mev, 100 kw, cw metric wave electron accel-
erator.
*Nuclear Instruments and Methods in Physics Research Section B:
Beam Interactions with Materials and Atoms*, 79(1–4):865–870,
June 1993.
ISSN 0168-583X.
doi: 10.1016/0168-583x(93)95487-p.
URL [http://dx.doi.org/10.1016/0168-583X\(93\)95487-P](http://dx.doi.org/10.1016/0168-583X(93)95487-P).
- [30] S. et al. Agostinelli.
Geant4—a simulation toolkit.
*Nuclear Instruments and Methods in Physics Research Section A: Ac-
celerators, Spectrometers, Detectors and Associated Equipment*,
506(3):250–303, July 2003.
ISSN 0168-9002.
doi: 10.1016/S0168-9002(03)01368-8.
URL [http://dx.doi.org/10.1016/S0168-9002\(03\)01368-8](http://dx.doi.org/10.1016/S0168-9002(03)01368-8).
- [31] VN Ivanchenko.
Geant4: physics potential for hep instrumentation.
*Nuclear Instruments and Methods in Physics Research Section A: Ac-
celerators, Spectrometers, Detectors and Associated Equipment*,
494(1-3):514–519, 2002.
- [32] Sylvain Meylan, Ulysse Vimont, Sébastien Incerti, Isabelle Clairand,
and Carmen Villagrasa.
Geant4-dna simulations using complex dna geometries generated by
the dnafabric tool.
Computer Physics Communications, 204:159–169, 2016.

- [33] L. Sostero, D. Pagano, I. Bodini, G. Bonomi, A. Donzella, D. Paderno, C. Pasini, V. Villa, and A. Zenoni.
Investigating the possibility of leakage detection in water distribution networks using cosmic ray neutrons in the thermal region.
Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, 1059:168951, February 2024.
ISSN 0168-9002.
doi: 10.1016/j.nima.2023.168951.
URL <http://dx.doi.org/10.1016/j.nima.2023.168951>.
- [34] C. M. Poole, I. Cornelius, J. V. Trapp, and C. M. Langton.
A CAD Interface for GEANT4.
Australasian Physical & Engineering Science in Medicine, September 2012.
doi: 10.1007/s13246-012-0159-8.
URL <http://www.springerlink.com/content/u563877422284578>.
- [35] Anton V. Ivantchenko, Vladimir N. Ivanchenko, Jose-Manuel Quesada Molina, and Sebastien L. Incerti.
Geant4 hadronic physics for space radiation environment.
International Journal of Radiation Biology, 88(1–2):171–175, September 2011.
ISSN 1362-3095.
doi: 10.3109/09553002.2011.610865.
URL <http://dx.doi.org/10.3109/09553002.2011.610865>.
- [36] Geant4: Guide for physics list.
https://www.fe.infn.it/u/paterno/Geant4_tutorial/slides_further/guide/.
- [37] iia EB-X Working Group.
Accelerators for sterilization of medical devices.
https://iiaglobal.com/wp-content/uploads/2021/09/Prospective-Accelerator-Buyer-Guide-6-May-2021-1.pdf?utm_source=chatgpt.com, 2021.
- [38] Yu.S. Pavlov, P.A. Bystrov, and O.N. Nepomnyaschy.
Optimization of accelerator beam scanning parameters to improve the efficiency of radiation technologies.
Radiation Physics and Chemistry, 177:109129, December 2020.

ISSN 0969-806X.

doi: 10.1016/j.radphyschem.2020.109129.

URL <http://dx.doi.org/10.1016/j.radphyschem.2020.109129>.

- [39] F. R. Studenikin, U. A. Bliznyuk, A. P. Chernyaev, G. A. Krusanov, A. D. Nikitchenko, S. A. Zolotov, and V. S. Ipatova.

Electron beam modification for improving dose uniformity in irradiated objects.

The European Physical Journal Special Topics, 232(10):1631–1635, June 2023.

ISSN 1951-6401.

doi: 10.1140/epjs/s11734-023-00886-6.

URL <http://dx.doi.org/10.1140/epjs/s11734-023-00886-6>.

- [40] Florent Kuntz.

Dosimetrie appliquee aux techniques d'ionisation par faisceaux d'electrons, 1991.

- [41] Simon Coenen.

Radiation Effects on Polymers.

SCK CEN, 1995.

- [42] Robert Bolt and James Carroll.

Radiation Effects on Organic Materials.

Academic Press, New York, 1963.

- [43] Wendy Wangsgard and Martell Winters.

Validation of a sterilization dose for products manufactured using a 3d printer.

Radiation Physics and Chemistry, 143:38–40, February 2018.

ISSN 0969-806X.

doi: 10.1016/j.radphyschem.2017.09.014.

URL <http://dx.doi.org/10.1016/j.radphyschem.2017.09.014>.

- [44] Paweł Rynio, Katarzyna Galant, Łukasz Wójcik, Bartłomiej Grygorcewicz, Arkadiusz Kazimierczak, Aleksander Falkowski, Piotr Gutowski, Barbara Dołęgowska, and Miłosz Kawa.

Effects of sterilization methods on different 3d printable materials for templates of physician-modified aortic stent grafts used in vascular surgery—a preliminary study.

- International Journal of Molecular Sciences*, 23(7):3539, March 2022.
ISSN 1422-0067.
doi: 10.3390/ijms23073539.
URL <http://dx.doi.org/10.3390/ijms23073539>.
- [45] Felix Horst, Elke Beyreuther, Elisabeth Bodenstein, Sebastian Gantz, Diego Misseroni, Nicola M. Pugno, Christoph Schuy, Francesco Tommasino, Uli Weber, and Jörg Pawelke.
Passive sobp generation from a static proton pencil beam using 3d-printed range modulators for flash experiments.
Frontiers in Physics, 11, July 2023.
ISSN 2296-424X.
doi: 10.3389/fphy.2023.1213779.
URL <http://dx.doi.org/10.3389/fphy.2023.1213779>.
- [46] Lorenzo Sostero, Matteo Ferrari, Davide Pagano, Stefano Pandini, Chiara Pasini, Aziz Boukenter, Adriana Morana, and Sylvain Girard.
Radiation-induced effects on commercial 3d printing materials exposed to high x-ray doses.
Journal of Physics: Materials, May 2025.
ISSN 2515-7639.
doi: 10.1088/2515-7639/addb7d.
URL <http://dx.doi.org/10.1088/2515-7639/addb7d>.
- [47] M.A.A. AlMaadeed, D. Ponnammma, and M.A. Carignano.
Polymer Science and Innovative Applications: Materials, Techniques, and Future Developments.
Elsevier, 2020.
ISBN 9780128173039.
URL <https://books.google.it/books?id=xpngDwAAQBAJ>.
- [48] Michel Biron.
Thermal Properties, page 339–375.
Elsevier, 2016.
ISBN 9780702062841.
doi: 10.1016/b978-0-7020-6284-1.00008-8.
URL <http://dx.doi.org/10.1016/B978-0-7020-6284-1.00008-8>.
- [49] Md Kamrul Hasan, David Staack, Suresh D. Pillai, Leonard S. Fifield, and Matt Pharr.

- Connecting radiation-driven changes in structural, thermal, and mechanical properties in several medical device polymers.
Polymer Degradation and Stability, 221:110677, March 2024.
ISSN 0141-3910.
doi: 10.1016/j.polymdegradstab.2024.110677.
URL <http://dx.doi.org/10.1016/j.polymdegradstab.2024.110677>.
- [50] Gérard Audran, Samuel Dorey, Nathalie Dupuy, Fanny Gaston, and Sylvain R.A. Marque.
Degradation of γ -irradiated polyethylene-ethylene vinyl alcohol-polyethylene multilayer films: An esr study.
Polymer Degradation and Stability, 122:169–179, December 2015.
ISSN 0141-3910.
doi: 10.1016/j.polymdegradstab.2015.10.021.
URL <http://dx.doi.org/10.1016/j.polymdegradstab.2015.10.021>.
- [51] Vasile C. and Butnaru E.
Radiation chemistry of organic solids.
ERASMUS book, 2016.
- [52] AAMI TIR17 et al.
Compatibility of materials subject to sterilization.
Arlington, VA: Association for the Advancement of Medical Instrumentation, 2017.
- [53] Ashley R. Jones, Arron Griffiths, Malcolm J. Joyce, Barry Lennox, Simon Watson, Jun-ichi Katakura, Keisuke Okumura, Kangsoo Kim, Michio Katoh, Kazuya Nishimura, and Ken-ichi Sawada.
On the design of a remotely-deployed detection system for reactor assessment at fukushima daiichi.
In *2016 IEEE Nuclear Science Symposium, Medical Imaging Conference and Room-Temperature Semiconductor Detector Workshop (NSS/MIC/RTSD)*. IEEE, October 2016.
doi: 10.1109/nssmic.2016.8069713.
URL <http://dx.doi.org/10.1109/NSSMIC.2016.8069713>.
- [54] Horatio Martin, Simon Watson, Barry Lennox, and Xavier Poteau.
Miniature inspection robot for restricted access exploration (mirrax).
In *WM Symposia*, volume 2018, 2018.

- [55] Behzad Rankouhi, Fereidoon Delfanian, Robert McTaggart, and Todd Letcher.
An experimental investigation of the effects of gamma radiation on 3d printed abs for in-space manufacturing purposes.
In *Volume 1: Advances in Aerospace Technology*, IMECE2016. American Society of Mechanical Engineers, November 2016.
doi: 10.1115/imece2016-67745.
URL <http://dx.doi.org/10.1115/IMECE2016-67745>.
- [56] Thomas McGuire, Michael Hirsch, Michael Parsons, Skye Leake, and Jeremy Straub.
Design for an in-space 3d printer.
In Khanh D. Pham and Genshe Chen, editors, *Sensors and Systems for Space Applications IX*. SPIE, May 2016.
doi: 10.1117/12.2223536.
URL <http://dx.doi.org/10.1117/12.2223536>.
- [57] Gavin Poludniowski, Artur Omar, Robert Bujila, and Pedro Andreo.
Technical note: Spekpy v2.0—a software toolkit for modeling x-ray tube spectra.
Medical Physics, 48(7):3630–3637, June 2021.
ISSN 2473-4209.
doi: 10.1002/mp.14945.
URL <http://dx.doi.org/10.1002/mp.14945>.
- [58] Tatsuhiko Sato, Yosuke Iwamoto, Shintaro Hashimoto, Tatsuhiko Ogawa, Takuya Furuta, Shin-ichiro Abe, Takeshi Kai, Pi-En Tsai, Norihiro Matsuda, Hiroshi Iwase, Nobuhiro Shigyo, Lembit Sihver, and Koji Niita.
Features of particle and heavy ion transport code system (phits) version 3.02.
Journal of Nuclear Science and Technology, 55(6):684–690, January 2018.
ISSN 1881-1248.
doi: 10.1080/00223131.2017.1419890.
URL <http://dx.doi.org/10.1080/00223131.2017.1419890>.
- [59] Arup Dey, Isnala Nanjin Roan Eagle, and Nita Yodo.
A review on filament materials for fused filament fabrication.

Journal of Manufacturing and Materials Processing, 5(3):69, June 2021.
ISSN 2504-4494.
doi: 10.3390/jmmp5030069.
URL <http://dx.doi.org/10.3390/jmmp5030069>.

- [60] C.V. Pious and Sabu Thomas.
Polymeric Materials—Structure, Properties, and Applications, page 21–39.
Elsevier, 2016.
doi: 10.1016/b978-0-323-37468-2.00002-6.
URL <http://dx.doi.org/10.1016/B978-0-323-37468-2.00002-6>.
- [61] Agnieszka Haryńska, Iga Carayon, Paulina Kosmela, Kamil Szeliski, Marcin Łapiński, Marta Pokrywczyńska, Justyna Kucińska-Lipka, and Helena Janik.
A comprehensive evaluation of flexible fdm/fff 3d printing filament as a potential material in medical application.
European Polymer Journal, 138:109958, September 2020.
ISSN 0014-3057.
doi: 10.1016/j.eurpolymj.2020.109958.
URL <http://dx.doi.org/10.1016/j.eurpolymj.2020.109958>.
- [62] Pratiksha Awasthi and Shib Shankar Banerjee.
Fused deposition modeling of thermoplastic elastomeric materials: Challenges and opportunities.
Additive Manufacturing, 46:102177, October 2021.
ISSN 2214-8604.
doi: 10.1016/j.addma.2021.102177.
URL <http://dx.doi.org/10.1016/j.addma.2021.102177>.
- [63] Rongrong Luo, Daoan Kang, Chao Huang, Tengfei Yan, Pengyuan Li, Hongxi Ren, and Zhiyuan Zhang.
Mechanical properties, radiation resistance performances, and mechanism insights of nitrile butadiene rubber irradiated with high-dose gamma rays.
Polymers, 15(18):3723, September 2023.
ISSN 2073-4360.
doi: 10.3390/polym15183723.
URL <http://dx.doi.org/10.3390/polym15183723>.

- [64] Andreea Madalina Pandele, Andreea Constantinescu, Ionut Cristian Radu, Florin Miculescu, Stefan Ioan Voicu, and Lucian Toma Cio-can.
Synthesis and characterization of pla-micro-structured hydroxyapatite composite films.
Materials, 13(2):274, January 2020.
ISSN 1996-1944.
doi: 10.3390/ma13020274.
URL <http://dx.doi.org/10.3390/ma13020274>.
- [65] Paul Wady, Alex Wasilewski, Lucy Brock, Ruth Edge, Aliaksandr Baidak, Connor McBride, Laura Leay, Arron Griffiths, and Cristina Vallés.
Effect of ionising radiation on the mechanical and structural properties of 3d printed plastics.
Additive Manufacturing, 31:100907, January 2020.
ISSN 2214-8604.
doi: 10.1016/j.addma.2019.100907.
URL <http://dx.doi.org/10.1016/j.addma.2019.100907>.
- [66] Markos Petousis, Nikolaos Michailidis, Vassilis M. Papadakis, Apostolos Korlos, Nikolaos Mountakis, Apostolos Argyros, Evgenia Dimitriou, Chrysa Charou, Amalia Moutsopoulou, and Nectarios Vidakis.
Optimizing the rheological and thermomechanical response of acrylonitrile butadiene styrene/silicon nitride nanocomposites in material extrusion additive manufacturing.
Nanomaterials, 13(10):1588, May 2023.
ISSN 2079-4991.
doi: 10.3390/nano13101588.
URL <http://dx.doi.org/10.3390/nano13101588>.
- [67] Conrad West, Robert McTaggart, Todd Letcher, Douglas Raynie, and Ranen Roy.
Effects of gamma irradiation upon the mechanical and chemical properties of 3d-printed samples of polylactic acid.
Journal of Manufacturing Science and Engineering, 141(4), February 2019.
ISSN 1528-8935.
doi: 10.1115/1.4042581.

URL <http://dx.doi.org/10.1115/1.4042581>.

- [68] Tomás J. Madera-Santana, R. Meléndrez, Gerardo González-García, Patricia Quintana-Owen, and Suresh D. Pillai.

Effect of gamma irradiation on physicochemical properties of commercial poly(lactic acid) clamshell for food packaging.

Radiation Physics and Chemistry, 123:6–13, June 2016.

ISSN 0969-806X.

doi: 10.1016/j.radphyschem.2016.02.001.

URL <http://dx.doi.org/10.1016/j.radphyschem.2016.02.001>.

- [69] A Babanalbandi, DJT Hill, DS Hunter, and L Kettle.

Thermal stability of poly(lactic acid) before and after γ -radiolysis.

Polymer International, 48(10):980–984, October 1999.

ISSN 1097-0126.

doi: 10.1002/(sici)1097-0126(199910)48:10<980::aid-pi257>3.0.co;2-b.

URL [http://dx.doi.org/10.1002/\(SICI\)1097-0126\(199910\)48:10<980::AID-PI257>3.0.CO;2-B](http://dx.doi.org/10.1002/(SICI)1097-0126(199910)48:10<980::AID-PI257>3.0.CO;2-B).