Faculdade de Ciências e Tecnologia da Universidade de Coimbra

Dose Optimization in CT, in Nuclear Medicine and in PET-CT Procedures

Thesis submitted

in fulfillment of the requirements

to obtain the Master's Degree in Biomedical Engineering

Ana Teresa Casimiro Nunes

2010/2011

Faculdade de Ciências e Tecnologia da Universidade de Coimbra

Dose Optimization in CT, in Nuclear Medicine and in PET-CT Procedures

Ana Teresa Casimiro Nunes

Thesis supervised by:

Pedro Vaz, Ph.D.

Instituto Tecnológico Nuclear

Paula Madeira, M.Sc.

Centro Hospitalar de Lisboa Central

Isabel Lopes, Ph.D.

Faculdade de Ciências e Tecnologia da Universidade de Coimbra

2010/2011

Hosting Institutions

Instituto Tecnológico Nuclear

Centro Hospitalar de Lisboa Central

Visited Institutions

"Hospital H1"

"Hospital H2" [1]

Hospital de São José

Hospital dos Lusíadas

Hospital da Luz

Hospital Garcia de Orta

Hospital Companhia União Fabril (Descobertas)

Instituto das Ciências Nucleares Aplicadas à Sáude

Hospitais da Universidade de Coimbra

[1] For the sake of confidentiality of data, "Hospital H1" and "Hospital H2" are not identified.

To my parents and my brother

DISCLAIMER

In the framework of the work reported in this thesis, several Nuclear Medicine and Radiology departments in Portuguese hospitals were visited. The clinical data that was kindly made available was of paramount importance for the objectives pursued in this study. The conclusions drawn in this study would not have been possible without the discussions held and the exchanges with the professionals (medical doctors, medical physicists, radiographers) and the *in loco* experience gained concerning the operational aspects of the equipments (tomographs, PET-CT scanners, etc.) and infrastructures and associated medical practices.

For the sake of confidentiality of data, professionals and patients of these institutions will not be explicitly identified in this work, nor will the provided data be correlated with its origin.

Acknowledgements

First and foremost, the author would like to thank her Thesis' advisors, Drs. Pedro Vaz and Paula Madeira, for their kind support and motivation, all through the execution of this work. She is also very grateful for their availability, comments and suggestions, which played a key role in the results and conclusions of this work.

The author also thanks her Professors, Isabel Lopes and Miguel Morgado, for the general supervision of this work. A special recognition goes to the housing institutions of the present Master Project - Instituto Tecnológico e Nuclear, Centro Hospitalar de Lisboa Central and Faculdade de Ciências e Tecnologia da Universidade de Coimbra, which made this work possible.

A major part of the work presented was made possible due to the contribution of the visited Nuclear Medicine and Radiology departments; the author gratefully acknowledges their availability, and the accompaniment provided within the respective facilities. The author is also indebted to the professionals of those same institutions, for the time they kindly afforded in order to respond to all her questions.

The author thanks to her colleagues, in particular to Ana Luísa Neves and Mariana Rufino, for the companionship and the fruitful exchange of ideas.

Last but not the least, the author is immensely grateful to her friends and family, for the unconditional support.

Abstract

The fast development during the last decades of medical imaging technologies, particularly, Computed Tomography, conventional Nuclear Medicine modalities and PET, PET/CT and other hybrid systems led to the exposure of patients, workers and members of the public to increasingly higher ionizing radiation doses and is a cause of concern, worldwide. The assessment of the radiation doses to which individuals are exposed in the context of the medical applications of ionizing radiation is of particular importance. Additionally, the dissemination, widespread utilization and prescription of medical examinations using ionizing radiation ultimately lead to a considerable collective dose.

The assessment of the (radiological) risk versus benefit, arising from the utilization of ionizing radiations for medical imaging purposes, must be performed in light of the three fundamental principles of the international system of Radiation Protection, namely justification, optimization and dose limitation. The state-of-the-art on the scientific knowledge associated to the effects of ionizing radiation in biological systems and potential detrimental aspects associated to the exposure of individuals to ionizing radiation led over the decades to the establishment of recommendations by international institutions (ICRP, IAEA) of good practices to promote and implement the safe utilization of ionizing radiations in clinical environments. In this context, the consequences and operational aspects of the implementation of the optimization principle in clinical environments involve complex tasks, linked to scientific, technical, societal, socio-economic, ethical and regulatory issues. The main goal of such implementation is to achieve, in most cases, the reduction of the doses to the patients, workers and members of the public.

For the purposes of the present work, nine Radiology and Nuclear Medicine medical institutions were visited in order to assess the exposure of patients, workers, and members of the public to radiation doses in Computed Tomography, conventional Nuclear Medicine and PET/CT examinations.

In the visited Nuclear Medicine services, it was possible to get acquainted with different equipments and practices and to analyze the real-time implementation of the Radiation Protection principles, of the radiation safety standards and good practices in conventional Nuclear Medicine and PET/CT examinations. Emphasis was mainly devoted to the doses to the workers and to a smaller extent to the doses to the patients.

In the visited Radiology services, dosimetric information data on the performed Computed Tomography examinations were retrieved, compiled and analyzed. Emphasis was given to patient doses.

In both types of services (Nuclear Medicine and Radiology services), the implemented dose optimization and Radiation Protection practices, methodologies and protocols were studied, and the processes requiring optimization were identified. In particular, for Computed Tomography procedures, the mean effective doses to which adult and pediatric patients are exposed were estimated, in head examinations.

Keywords: Computed Tomography, Nuclear Medicine, PET-CT, Dose Optimization, Radiation Protection.

Resumo

O desenvolvimento de novas tecnologias de imagem médica, em particular a Tomografia Computorizada, as técnicas convencionais de Medicina Nuclear e PET, PET/CT e outros sistemas híbridos, tem levado à exposição de doentes, trabalhadores e membros do público a doses progressivamente mais elevadas de radiação ionizante, o que representa um motivo de preocupação, a nível mundial. O estudo das doses de radiação a que são expostos estes indivíduos, no contexto das aplicações médicas da radiação ionizante, revela ser de particular importância. Adicionalmente, a repetição e prescrição frequentes deste tipo de exames médicos pode levar a uma dose de radiação colectiva consideravelmente elevada.

O estudo do risco *versus* benefício, resultantes da utilização da radiação ionizante em imagiologia médica, deve ser efectuado à luz dos três princípios fundamentais do sistema internacional da Protecção Radiológica, nomeadamente a justificação, a optimização e a limitação da dose. O estado-da-arte do conhecimento científico no que respeita aos efeitos da radiação ionizante em sistemas biológicos e aos potenciais efeitos prejudiciais associados à exposição de indivíduos à radiação ionizante tem levado, nas últimas décadas, ao contínuo estabelecimento de recomendações por instituições internacionais (ICRP, IAEA) de boas práticas de utilização segura de radiações ionizantes, a promover e implementar em ambiente hospitalar. Neste contexto, as consequências e os aspectos operacionais da implementação do princípio da optimização em ambiente clínico envolvem tarefas complexas, ligadas a factores científicos, técnicos, socioeconómicos, éticos e reguladores. O principal objectivo de tal implementação é atingir, na maior parte dos casos, uma redução das doses para os doentes, trabalhadores e membros do público.

No âmbito do presente trabalho, nove instituições médicas de Radiologia e Medicina Nuclear foram visitadas, com o intuito de estudar a exposição de doentes, trabalhadores e membros do público a doses de radiação ionizante em exames de Tomografia Computorizada, de Medicina Nuclear Convencional e de PET/CT.

Nos Serviços de Medicina Nuclear visitados, houve a oportunidade de assistir à implementação, em tempo real, dos princípios e boas práticas de Protecção Radiológica em exames de Medicina Nuclear convencional e de PET/CT, tendo sido dada especial atenção às doses dos trabalhadores expostos.

Nos Serviços de Radiologia foi possível aceder a bases de dados com informação dosimétrica relativa a exames de Tomografia Computorizada realizados, tendo sido dada mais importância às doses dos doentes.

Em ambos os tipos de Serviço (Medicina Nuclear e Radiologia), foi efectuado o levantamento das diferentes práticas de optimização de dose e de Protecção Radiológica implementadas, estudaram-se as metodologias e protocolos em uso e identificaram-se os pontos a optimizar. Para os exames de Tomografia Computorizada, em particular, estimaram-se as doses efectivas a que, em média, estão expostos doentes adultos e pediátricos em exames de crânio.

List of Acronyms

ACR - American College of Radiology

ALARA – "As Low As Reasonably Achievable"

BEIR – Biological Effects of Ionizing Radiation (Committee)

BGO – Bismuth Germanate

CT – Computed Tomography

CTDI – Computed Tomography Dose Index

$CTDI_{100}$ – Computed Tomography Dose Index, for a 100 mm length pencil ion chamber

$CTDI_{vol}$ – Volumetric Computed Tomography Dose Index

$CTDI_{w}$ – Weighted Computed Tomography Dose Index

DLP – Dose-Length Product

DRL – Diagnostic Reference Level

E – Effective Dose

EANM – European Association of Nuclear Medicine

EURATOM – European Atomic Energy Community

FDA – Food and Drug Administration

FDG – Fluoro-2-deoxyglucose

FOV – Field-of-View

GE – General Electric

GSO – Gadolinium Orthosilicate

H_T – Equivalent Dose

HMPAO – ^{99m}Tc-Hexamethylpropyleneamine Oxime

$H_p(0,07)$ – Skin equivalent dose (body depth of 0,07 mm)

$H_p(10)$ – Average equivalent dose (body depth of 10 mm)

IAEA – International Atomic Energy Agency

ICRP – International Commission on Radiological Protection

IEC – International Electrotechnical Commission

LET – Linear Energy Transfer

LOR – Line of Response

LSO – Leutetium Orthosilicate

MAA – ^{99m}Tc-Albumin Aggregated

MAG3 – ^{99m}Tc-Mercaptoacetyltriglycine

MDP – ^{99m}Tc-Methyldiphosphonate

MIRD – Medical International Radiation Dose (Committee)

MRI – Magnetic Resonance Imaging

MTPA – 99mTc-Diethylene Triamine Pentaacetic Acid

NaI(Tl) – Thallium-doped Sodium Iodide

NCRP – National Council on Radiation Protection & Measurements

PACS – Picture Archiving and Communication System

PDU – Power Distribution Unit

PEM - Positron Emission Mammography

PET – Positron Emission Tomography

PET/CT - Positron Emission Tomography/Computed Tomography

PMMA – Polymethylmethacrylate

PMT – Photomultiplier Tube

RERF – Radiation Effects Research Foundation

SI – Système International (d'unités)

SPECT – Single Photon Emission Computed Tomography

$\mathbf{T_{1/2}}$ – Physical Half-Life

UNSCEAR – United Nations Scientific Committee on the Effects of Atomic Radiation

$\mathbf{W_R}$ – Radiation Weighting Factor

$\mathbf{W_T}$ - Tissue Weighting Factor

Table of Contents

List of Figures

List of Tables

1. Introduction

Ionizing radiation is defined as a type of radiation which is energetic enough to eject electrons from atoms or molecules. The molecules containing unpaired electrons (free radicals) resulting from an ionization process are usually very chemically reactive, easily interacting with the surrounding medium. For this reason, the interaction between ionizing radiation and biological tissues and organs may affect the DNA structure, the cellular mechanisms and potentially cause harmful effects on living organisms. Besides being exposed to natural sources of ionizing radiation, individuals are frequently exposed to radiation from various artificial sources, used for industrial, research and particularly medical purposes, amongst others. In fact, ionizing radiation represents today a valuable, widely used tool in a range of medical applications - diagnostic and interventional Radiology, Nuclear Medicine and Radiotherapy.

The data available from epidemiological studies is the starting point for the assessment of the risk associated to the exposure of individuals to ionizing radiation. One of the major sources of epidemiologic data for radiological risk assessment has been the study of the atomic bomb survivors in Hiroshima and Nagasaki, in 1945. As more radiation-exposed populations have been studied in the past few decades, risk estimates have been generally consistent with those of the atomic bomb survivors. The data from these epidemiologic studies is also supported by experimental biology and other experimental studies at the molecular and cellular level [1,2]. Similar conclusions between the numerous experimental studies performed and the epidemiological data available indicate that even though the mechanisms that lead to detrimental health effects after exposure to ionizing radiation are yet to be fully understood, there is evidence that occurrence of solid cancer, as well as other health effects, increases proportionally to radiation dose [3]. The cancer induction risk is well accepted, although there is controversy over risks at low doses rates. Studies have shown a linear correlation in the number of excess tumors to the dose of the exposure, that is, as the amount of exposure is increased, the number of excess tumors also increases. It also appears that no low-dose threshold exists for the induction of cancers [4]. Cancer induction due to radiation exposure can take several years to manifest and it isn't certain how the levels of ionizing radiation a patient is exposed to cause that induction effect. From the perspective of radiation safety

alone, it surely makes sense to withhold an imaging procedure using ionizing radiation in order to reduce radiation dose to the patient but, in a more global risk-benefit analysis, it is reasonable to expose the patient to low levels of ionizing radiation, if not having the necessary diagnostic information represents a superior risk for the patient's health [5]. Therefore, if an imaging procedure is *justified* for diagnostic purposes and as long as the radiation dose for the patient is correctly *optimized*, there is no reason not to perform the examination. Hence, diagnostic imaging procedures are being gradually more prescribed by physicians in the current days, already representing one of the greatest sources of exposure to ionizing radiations.

Over the last three decades, there has been a worldwide increase in the number of the performed medical procedures that deliver ionizing radiation to patients. In particular, diagnostic examinations such as CT and Nuclear Medicine examinations [6] deliver higher doses (factor of 100 in some cases) than those typically considered in Conventional Radiology examinations. For instance, according to an NCRP report (Report No. 160, *Ionizing Radiation Exposure of the Population of the United States* [7]*)*, a significant increase was observed in the medical radiation exposure of the USA population during the period between the early 1980s and 2006. Figure 1.1 illustrates this situation, comparing the fraction of medical-related exposures during this period to the overall exposure of the aforementioned population:

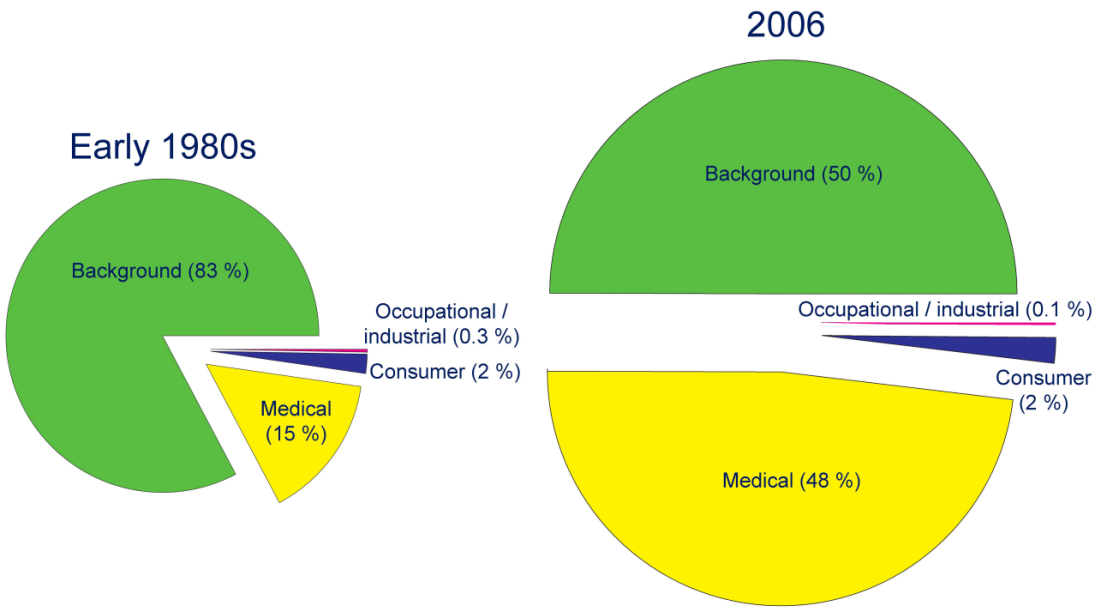


Figure 1.1 – Evolution of the radiation exposure of the USA population, between the 1980-decade and 2006. From [8].

As can be seen on the previous figure, in 2006, medical exposure to ionizing radiation constituted about 48% of the total radiation exposure of the USA population, considering all natural and artificial sources. This marked increase was primarily due to the dissemination of the use of CT and Nuclear Medicine imaging procedures, that accounted for 24% and 12% of the total exposure, respectively, as depicted in Figure 1.2. In fact, these two modalities accounted for 75% of the medical radiation exposure of the USA population. Accordingly, the number of CT scans and Nuclear Medicine procedures performed during the year of 2006 was estimated to be in the order of 67 million and 18 million, respectively [7].

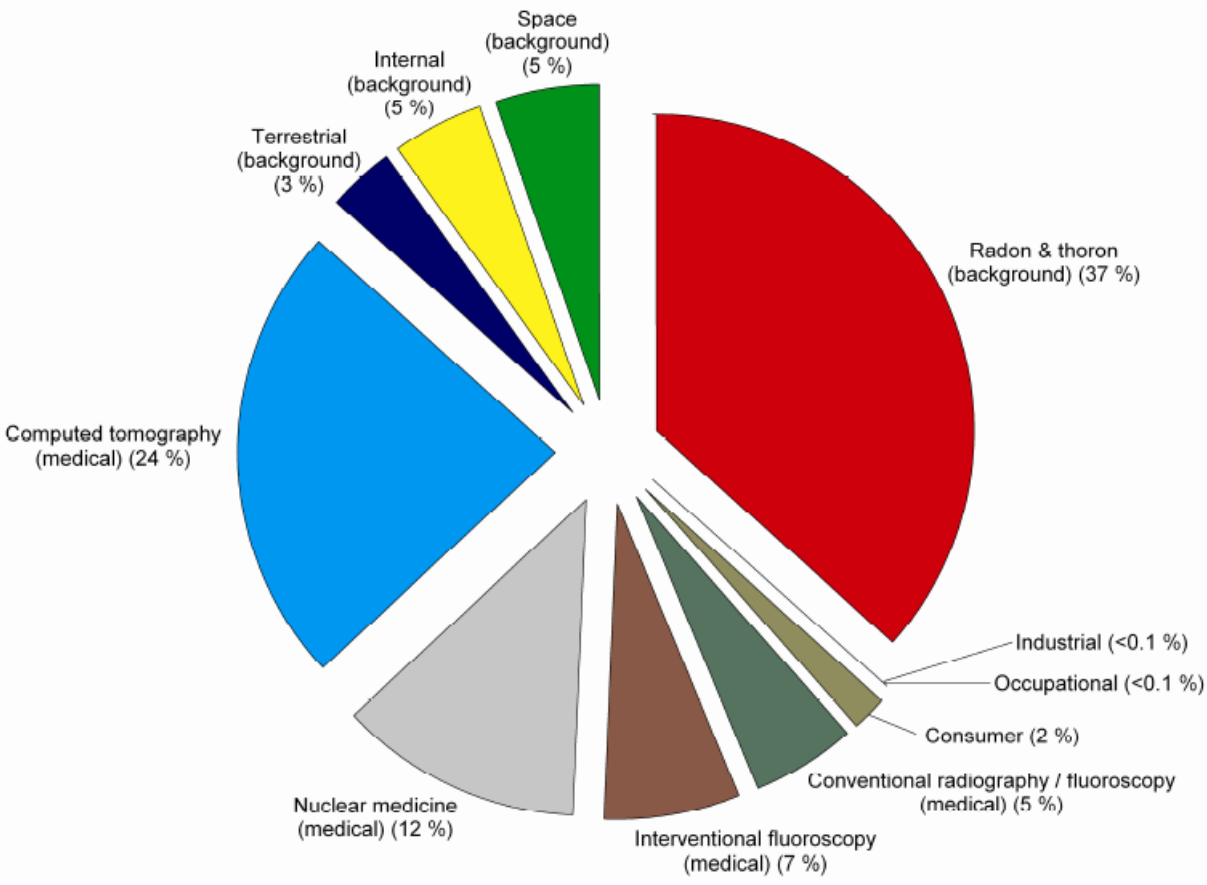


Figure 1.2 – Relative exposure from all ionizing radiation sources, for the USA population, during the year of 2006. From [7].

Throughout the year of 2007, medicine represented the largest source of radiation exposure to the USA population [6] and today medical applications of ionizing radiation constitute the main artificial source to population exposure. Annually, there are more than 3,600 million diagnostic

x-ray and 37 million Nuclear Medicine examinations performed worldwide and, in addition to the exposed patients, about 7 million health professionals are exposed to ionizing radiation [9]. The increasing demand for radiological and Nuclear Medicine medical imaging procedures, in particular, has resulted in a higher exposure of the overall population, including both medical and occupational exposures. Given the magnitude of the exposed population to ionizing radiation, it is clear that the implementation of Radiation Protection-aimed practices, particularly in medical context, is of the upmost need.

Constant technological advances during the past few decades led to a remarkable progress in image quality, scan time and diagnostic precision, contributing for the ever-growing amount of CT scans performed. In Nuclear Medicine, whether for conventional examinations, or PET and SPECT procedures, the growing availability of scanning equipment and the continuous introduction of new radiopharmaceuticals have led to an increase in the number of examinations. Additionally, the use of new hybrid imaging technologies, particularly PET/CT systems, is promptly expanding [10]. The combination of anatomical information available from CT scans and of molecular and/or functional information (provided by PET or SPECT) provides a superior diagnostic value with various clinical applications, but the internal dose delivered by the administered radiopharmaceuticals adds to the external dose due to x-ray irradiation. In a general perspective, the technological progress in imaging modalities may be considered a double-edged sword. In principle, it is easier to limit the delivered radiation dose using advanced imaging systems, but often technical improvements focus on the enhancement in the image quality and do not necessarily lead to a decrease in the exposure to ionizing radiation.

The radiation doses delivered to patients undergoing CT, PET, SPECT and multimodal examinations are relatively low, but repeated procedures may lead to significant cumulative doses. This is particularly concerning in pediatric patients, owing to their higher tissue radiosensitivity and longer (and rising) life expectancy. Collective dose is also of great concern. The considerable number of medical imaging procedures may lead to a potentially severe Public Health problem, if a correct assessment of the risk versus benefit analysis is not performed. Such assessment has to take into consideration the fundamental principles of the international system of Radiation Protection and the international safety standards (published

by the IAEA) concerning the exposure to ionizing radiation of the patients, workers and members of the public.

Several international institutions such as the ICRP and the IAEA have introduced a framework for Radiation Protection and Safety, supported by scientific studies undertaken by the UNSCEAR (amongst other institutions). The ICRP has established the basic architecture and principles of the International System of Radiation Protection and periodically publishes and updates recommendations to be implemented in practice. According to the ICRP Publication 103, "*the probabilistic nature of stochastic effects of radiation makes it impossible to derive a clear distinction between 'safe' and 'dangerous', and this creates some difficulties in explaining the control of radiation risks*" [2], so the recommendations are to be viewed as practical and interventional guidelines, aimed at the appropriate management and control of exposures to ionizing radiation. The ICRP's system of Radiation Protection is based upon three fundamental principles:

- Justification (of practices),
- Optimization (of the protection) and
- Dose limitation.

In what concerns medical applications of ionizing radiation, the justification principle is related to the necessity of a clearly justified clinical prescription for the radiological exposure of the patient. The optimization principle refers to the well known ALARA principle: "As Low As Reasonably Achievable", which means that any radiation exposure must be kept as low as possible, without compromising the expected benefits of the use of said radiation e.g. the diagnostic accuracy and imaging quality, in the case of diagnostic applications. Finally, the third principle of Radiation Protection states that no exposure to ionizing radiation of workers and individual members of the public must exceed the established dose limits.

Various studies have been published on the radiation doses delivered in medical imaging examinations showing, as the already mentioned NCRP Report 160 [7], the relative importance of the different medical imaging modalities using ionizing radiation to the total collective dose in the USA. Several other studies undertaken in European countries (France [11], for instance) indicate an increasing contribution (in terms of dose and frequency of exams) of CT and

Nuclear Medicine to the total collective dose. In Europe, the Council Directive 97/43 of EURATOM [12] requires Member States to evaluate the collective radiation dose due to medical exposures. For instance, ten countries participated in a *DOSE DATAMED* project, which aims at collecting data on the doses delivered in radiological and Nuclear Medicine procedures in the EU. Therefore, in the USA and in some of the European countries, the radiation exposures due to medical purposes and the amount of imaging procedures performed are satisfactorily recorded, although significant discrepancies in dose results for different countries are evident [13]. However, this type of studies is not available in Portugal so far, and therefore it is fundamental to characterize the Portuguese situation in these matters.

The implementation of the optimization principle in the medical applications of ionizing radiations, namely for diagnostic imaging purposes, requires the assessment of the doses to which patients and workers are exposed. Its implementation is a complex task, as it interferes with the operational aspects of Radiation Protection in clinical environments and workplaces. Optimization strategies and methodologies can be achieved in multiple ways:

- A proper selection of the technical parameters (such as kV, mAs, pitch, etc.) and dose features (such as automatic exposure control, dose modulation, etc.) of the x-ray equipments;
- Appropriate manipulation and administration of the radiopharmaceuticals in Nuclear Medicine;
- Reducing the time of exposure;
- Increasing the distance to the radiation sources;
- Utilization of appropriate structural shielding (barriers) or of protective personal shielding (lead aprons, gloves, glove boxes, thyroid collars, protective glasses, etc.).

The interplay between Justification and Optimization principles is also complex, as properly justified examinations and avoidance of repeated prescriptions will necessarily lead to an optimized (reduced) dose to the patient.

In CT procedures, radiation dose can be estimated based on dosimetric quantities indicated by the equipment's software but, in order to assess the radiation risk, one must evaluate the correlation between those quantities and the actual patient dose. This can be done through

measurements where phantoms (representative of the human body) are irradiated at the nominal operating parameters (protocols), using adequate radiation detection equipment (pencil ionization chambers and electrometers). However, when dealing with radiopharmaceuticals in Nuclear Medicine procedures, dose estimations based on measurements are much more difficult to assess, as the *internal* exposure of several organs and tissues must be considered, and biokinetic models, specific to the incorporated radionuclides must be used.

In order to evaluate how dose optimization is put into practice, the standard imaging protocols in use must be studied. These protocols are customized by the medical institutions themselves and tailored to the equipment, examinations and patients involved. Furthermore, dose optimization depends on the correct implementation of those established protocols, which is sometimes overlooked, due to an insufficient education of the technicians involved.

While a few Portuguese publications suggesting new and optimized protocols for CT examinations have been published [14], in Nuclear Medicine and multimodality procedures studies of the exposure of patients, workers and members of the public are rare. The scarcity of published work on these subject matters served as the motivation for undertaking the studies reported in this thesis. More specifically, the medical imaging procedures studied in this work are, in diagnostic Radiology, CT and, in Nuclear Medicine, conventional exams and new hybrid medical technologies, particularly PET/CT systems. The objectives of this work are:

- To get acquainted with the existing equipments (tomographs, PET/CT scanners, etc.), practices (namely related to the handling, manipulation and administration of radioisotopes in Nuclear Medicine), protocols in use and their implementation and, more generally, with operational Radiation Protection aspects of the implemented clinical practices;
- To perform an assessment of the doses for the patient in CT, in conventional Nuclear Medicine and in PET/CT examinations;
- To evaluate the radiation exposure of workers and members of the public, in conventional Nuclear Medicine and in PET/CT services in Portugal;
- To study and characterize the implementation of Radiation Protection principles and recommendations of radiation safety principles and standards, in Radiology and Nuclear Medicines services in Portugal;

- To study the implemented optimization strategies and methodologies in Radiology and Nuclear Medicine services in Portugal;
- To formulate recommendations to be implemented in feasible protocols for Dose Optimization in clinical environments.

The present chapter introduces the scope of this thesis, including the objectives proposed and an overview of the various topics to be explored in the following chapters.

Chapter 2 succinctly discusses ionizing radiation related topics, such as the three Radiation Protection basic principles, radiosensitivity, dosimetry units and biological effects of ionizing radiation. The presentation of these topics is performed in view of the increasing awareness about the detrimental effects of radiation in biological tissues, and of the ever-growing dissemination of medical applications using ionizing radiations.

Chapter 3 focuses on the physical, technological and technical fundamentals of CT, Nuclear Medicine modalities and hybrid systems. History and evolution of these imaging techniques are briefly addressed, as well as their main diagnostic applications and the equipments' general structure, operation and parameters. The compromise between radiation dose and image quality is also included for each type of imaging modality, and the typical radiation doses patients are exposed to during these medical imaging examinations are indicated. In addition, for CT, the technical factors that influence patient dose and image quality are mentioned and, for Nuclear Medicine modalities, the most commonly used radioisotopes are listed.

In Chapter 4, the work specifically developed in this work is presented, consisting of a compilation, analysis and interpretation of data gathered at several Radiology and Nuclear Medicine services in Portugal. Additionally, dose optimization strategies, methodologies and Radiation Protection related practices implemented in these institutions are characterized. A dose optimization survey on conventional Nuclear Medicine and PET/CT practices was carried out and its conclusions are presented. This chapter also comprises a CT study, where dosimetric information on patient examinations is analyzed. The implications of both these studies are discussed in Chapter 5 and possible dose optimization and Radiation Protection-related practices and methodologies are suggested, for eventual implementation in clinical environments.

Finally, Chapter 6 summarizes the main conclusions to be extracted from the work undertaken and analyzed data. Suggestions for future work are provided.

2. Radiobiology, Radiosensitivity and Radiation Protection

2.1. Radiation Interaction with Matter

Ionizing radiation can actively interact with matter, delivering its kinetic or electromagnetic energy to any solid, liquid or gas material it passes through. Three possible outcomes can result from this interaction, depending on nature of the radiation and the composition of the matter [15,16]:

- No effect – radiation traverses matter without losing its energy to the surrounding medium and no interaction occurs;
- Radiation interacts with the matter's atoms outer shell electrons;
- Radiation interacts with the matter's atoms nuclei.

Let us first differentiate electromagnetic waves from accelerated particles. The interaction between gamma-ray and x-ray photons (included in the former category) and matter results in a decrease in the intensity (number of photons) of the primary beam which traverses matter – a process called **attenuation** [15], expressed by the following equation:

$$I = I_0 \cdot e^{-\mu x} \qquad \textbf{Equation 2.1}$$

where *I* is the photon beam's intensity at the point where the beam exits the segment of matter where attenuation occurs and I_0 the beam's intensity before it reached such segment. Additionally, attenuation depends on both the thickness (*x*) of the matter's segment and the attenuation coefficient μ - a quantity that characterizes how easily the material constituting the matter is penetrated - depending on the photon beam's intensity, thickness and average Z of the matter's segment [17]. Expectedly, this attenuation coefficient is greater for denser tissues (such as bone).

One of the processes through which radiation interacts with matter is *excitation*, where an inner-shell electron migrates to an outer-shell of the atom, which is then said to be in an excited state. In *ionization* processes, however, an electron is ejected from the atom [15,16].

A final aspect of radiation interaction with matter worth mentioning is the penetration power of radiation, that is, how deep radiation penetrates a material. Evidently, different types of radiation have different path lengths within matter. The **linear energy transfer** (LET) expresses the amount of transferred energy per unit of path length by a particle, while it traverses a sample of matter. This parameter, quantified in units of KeV/μm, is used to quantify the radiation's efficiency in producing biological damage. Alpha particles, for instance, due to their heavy mass and charge, rapidly interact with orbital electrons of the material´s atoms they traverse, degrading their energy in short distances. In fact, they have a path length of about 3–10 cm in air and 25–80 μm in biological tissues (or other solids in general). For this reason, they are classified as a high-LET type of radiation. Beta particles, conversely, are low LET radiation types: they are much more penetrating than alpha particles, having a path length of about 0–15 meters in air and of several millimeters in biological tissues. Finally, x- and gamma-ray photon beam's intensity decreases exponentially as it penetrates matter, as expressed in Equation **2.1** [15,16].

2.2. Biological Effects of Ionizing Radiation

2.2.1. Epidemiological Studies on Radiation Risks

There is currently plenty of information available on the biological effects of radiation, as a result of the numerous experimental animal studies and human epidemiological studies performed in the past few decades. The growing understanding of the different mechanisms of cellular responses to irradiation ultimately leads to theoretical studies on radiation-induced damage; however, the lack of definitive information force us to rely on human experience [18]. On the one hand, the aforementioned experimental studies, which comprise cellular, cytogenetic and molecular techniques, are often used to investigate radiation carcinogenesis, using rodent models. For instance, in what concerns leukemia and some solid tumors of the skin, bone, brain, lung, breast and gastro-intestinal tract, these animal studies provide evidence on how radiation induces carcinogenic processes, shedding light on the genetic mutations involved, which are also present in humans [2]. On the other hand, the gathered epidemiological data is, for the most part, obtained from studies performed to the Hiroshima and Nagasaki atomic bomb survivors. The Japanese Radiation Effects Research Foundation (RERF) has been conducting, over the decades, follow-up studies on cohorts of the Japanese bombings' survivors and their progenies [3].

Approximately 87,000 survivors have been followed since the bombings in 1945, in order to study the radiation-induced incidence of cancers, other diseases and mortality on those populations [1]. A marked increase of leukemia incidence has been observed for the irradiated populations [19], when compared with non-exposed populations (see Table 2.1):

Table 2.1 – Relative risk (radiation-induced occurrences over expected natural occurrences) of leukemia death for the exposed populations of Hiroshima and Nagasaki. Adapted from [19].

	Hiroshima	**Nagasaki**
Relative Risk	$\mathrm{RR} = \frac{61 \text{ leukemia deaths}}{12 \text{ expected cases}} = 5{,}08$	$\mathrm{RR} = \frac{61 \text{ leukemia deaths}}{12 \text{ expected cases}} = 2{,}85$

In addition to the Japanese atomic bombs' survivors, other irradiated populations have been studied over the last century. In the 1920s, radium watch dials painters were found to have an increased rate of bone cancer, compared with the natural incidence of that type of tumor. Later, in the 1940s, studies on the amplified leukemia incidence amongst radiologists were developed and, two decades later, quantitative estimates of lung cancer risk for underground radon miners were published. In addition, in the last half-century, several other human epidemiological studies assessed the carcinogenic risk of exposed populations within military, occupational and medical environments [1]. Finally, epidemiological data on the exposed population from the Chernobyl nuclear reactor incident, in 1986, is also being collected [18]. The "results" from all these studies ultimately lead to the determination of one important value: the cancer risk coefficient, which describes the average lifetime risk of fatal cancer per sievert (of effective dose). This coefficient has been estimated by several entities, including the ICRP, the NCRP, the UNSCEAR and the BEIR Committee [18].

The identification of radiation-induced cancers amongst a myriad of natural cancers presents a few limitations – the incidence of cancer might be owed to some external factor, such as smoking, nutrition and dietary factors or chemical pollution and not to the radiation exposure itself. Furthermore, the available evidence on the detrimental effects of radiation is mostly related to observations at high doses, as in the case of the Hiroshima and Nagasaki cohort studies. Conversely, most of the regular irradiations of concern, such as those from medical applications of ionizing radiation, occupational exposures and indoor radon, entail much lower dose levels [18]. In

fact, at low doses (defined by the BEIR Committee to be in the range of near zero up to approximately 100 mSv), statistical fluctuations obscure the determination of radiation cancer risk, for the main reason that, at low-doses, the number of radiation-induced cancers is very small [3]. For this reason, the rate of cancer induction risks at low doses is usually estimated by extrapolating from what is observed at higher doses. This extrapolation is made in terms of **dose–response curves**, which relate excessive cancer mortality to ionizing radiation doses [20]**:**

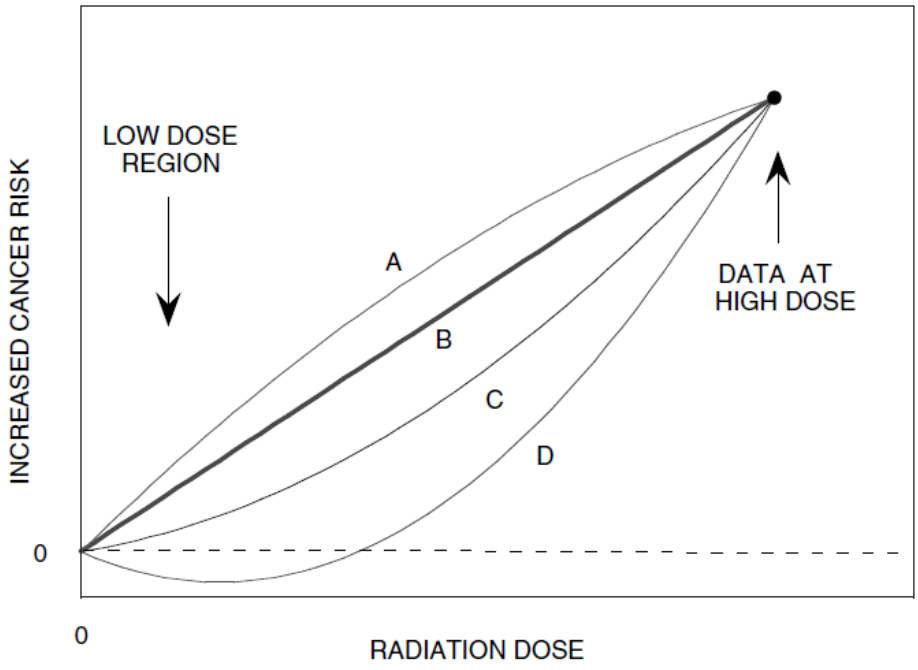


Figure 2.1 – Typical dose-response curves for cancer induction: supralinear (A), linear (B), linear-quadratic (C), and *hormesis* (D). From [18].

In Figure 2.1, different dose-response curves are depicted, correspondent to alternative assumptions for the extrapolation of the cancer induction risk *versus* radiation dose at low dose levels, from a known risk at higher doses. **Curve B** represents the dominant hypothesis: a linear relationship, with a specified threshold D_T, where the risk of cancer induction is proportional to the magnitude of the dose. Below that threshold level, there is no appreciable rate of cancer induction. An alternative to the linearity hypothesis is expressed by **Curve A**: greater effects than the ones implied by the linearity hypothesis occur at low dose levels. **Curve C** represents a linear-quadratic dose response, where the extrapolated risk is reduced at low dose levels, in comparison with the linearity hypothesis and **Curve D** assumes negative values at low doses, which corresponds to beneficial effects of small radiation doses (hormesis) [18,20].

It has been demonstrated that the exposure to ionizing radiation is also associated to an increased risk of non-cancer diseases, such as cardiovascular disease. In fact, heart disease and stroke episodes may occur at high radiation doses [3], but in order to quantify the non-cancer diseases risk at lower doses, additional epidemiological studies are underway.

In conclusion, regardless the significant amount of both epidemiological and experimental data, there is still a lack of knowledge on the radiation health risks. Although clear evidence exists about the radiation-induced cancer risk, several issues remain to be resolved, particularly the radiation risk at low doses. Due to its statistical nature, there will always be some ambiguity and limitations in the determination of radiation risk estimates [1].

2.2.2. Interaction of Ionizing Radiation with cells and with the DNA

The eventual biological damage is caused by physical interactions between radiation and specific structures within the cells. The key reason why ionizing radiation has such detrimental effects on biological tissues is associated to the interaction of radiation with deoxyribonucleic acid (DNA) sequences existing inside of the cell's nucleus, which contain vital genetic information and represent the most critical target within the cell. Other cell structures, when damaged, may also lead to functional complications [15,20]. The radiation damage to the cell occurs mainly through direct and indirect processes:

- **Direct interaction –** radiation directly interacts with a critical target within the cell. The atoms or molecules of the target are ionized or excited by means of Coulomb interactions, a process that fuels a sequence of chemical events, which eventually provoke the final biological damage. Direct interaction of radiation is the dominant process for extremely ionizing particles such as neutrons, protons and heavy charged particles [16,20].

- **Indirect interaction -** radiation interacts with other molecules (water, for instance) within the cell [20]. This process results in the formation of free radicals, which are extremely reactive molecules because they have an unpaired valence electron. These free radicals, in turn, can later damage critical targets in the cell. In particular, when ionizing radiation interacts with water molecules, free radicals such as water ions (H_2O^+) and hydroxyl radicals (OH•) are created. Although short-lived, these radicals are highly chemically unstable, and can spread

through the cell and interact with distant critical targets [16]. The biological detriment caused by sparsely ionizing radiation**,** such as x-rays or electrons, occurs predominantly through indirect processes of interaction.

2.2.3. Radiation Effects on Biological Tissues

An important distinction to make is the separation between low and high doses, as they evidently result in different effects on biological tissues. As defined in a few credited publications, such as the NCRP Report No. 136 and the BEIR VII Report [3], low to moderate doses encompass the values between 0 and 100 mSv, and high doses include values greater than 100 mSv. On the one hand, the lower the dose, the smaller the observed effect – in fact, for extremely low doses, the radiation induction of harmful effects is masked by their natural incidence. Very high radiation doses (above 2-3 Sv), on the other hand, are considered to be lethal [18]. The effects of ionizing radiation on biological tissues and organs are often categorized according to the required time for those damaging effects to manifest [21]:

- **Acute effects** occur within several hours or days after the exposure of the individual to extremely high doses;
- **Delayed or latent effects** manifest several weeks or years after the exposure.

Radiation effects are also classified as either deterministic or stochastic:

- **Deterministic effects** are expressed in the form of harmful tissue reactions, which mostly manifest after an exposure to high radiation doses. These types of effects are generally characterized by a threshold dose level, above which the severity of the radiation-induced lesion (which can eventually lead to a serious cellular malfunction, or cell death) increases linearly with dose [2]. Therefore, an increase on radiation dose will result in a direct amplification of the lesion severity, depending on the number of damaged cells [18].

- **Stochastic effects** include both carcinogenic and hereditary (genetic) effects and may occur following lesions on either one or various cells, without a threshold dose level. An increase on radiation dose will raise the effect's frequency or probability, but not its severity.

Finally, radiation effects can be summarized into three main categories:

- **Carcinogenic effects** involve some kind of cancer growth in the exposed individual's tissue, due to induced somatic mutations (as opposed to genetic mutations). Radiation exposure is strongly associated with the induction of leukaemia, thyroid, breast and lung cancers, in particular, and also with others types of cancer, such as stomach, oesophagus, bladder, lymphoma and salivary glands' tumours [22].

- **Non-carcinogenic effects** cover the "induction" of diseases other than cancer. A cohort study on Hiroshima and Nagasaki exposed populations, in particular, associates radiation exposure with the induction of heart disease, stroke, digestive disorders, and respiratory disease [**2**]. Induction of cataracts and vision impairment arising from damage caused to the lens of the eye are other type of non-carcinogenic effect caused by ionizing radiation.

- **Mutagenic effects** correspond to any serious or dominant mutation induced by radiation, as well as other genetic alterations [22]. Moreover, if a mutation occurs in the individual's reproductive (germ) cells, the heritable mutation effects can also affect his or her offspring [2].

2.2.4. Radiosensitivity

In 1906, J. Bergonie and L. Tribondeau observed the effects of ionizing radiation on cells, tissues and organs [23], and concluded that:

1. Stem cells are more sensitive than differentiated cells. The greater the differentiation stage of the cell, the greater its resistance to radiation effects;

2. Young organ and tissues are more radiosensitive than older, mature organs and tissues;

3. Superior metabolic activities are associated to greater levels of radiosensitivity;

4. A faster rate of cellular proliferation and tissue growth results in a greater radiosensitivity [24].

In addition, geneticist H.J. Muller, who studied the radiation's role in mutation (*mutagenesis*), discovered in 1927 that the genetic mutations induced by radiation are very much similar to the ones that naturally occur, only their frequency is greater [24].

Radiosensitivity is also dependent on the phase of the cellular cycle the cell is undergoing at the moment of irradiation: the most radiosensitive phase is the moment when mitosis occurs, and the most radioresistent cellular phase is phase S (when the cell's division process is temporarily latent). As for cellular structures, the nucleus is more radiosensitive than the cytoplasm and the DNA is the most critical, radiosentitive structure within the cell [22].

2.3. Radiation Protection and Dosimetry

2.3.1. Radiation Protection Principles

As mentioned earlier, radiation interaction with matter is materialized by an energy transfer process, which can excite or ionize atoms and molecules. It is the ionizing property of radiation and the previously discussed effects induced at the cellular and DNA level that potentially originate and induce the harmful and detrimental biological effects of ionizing radiation. The implementation of Radiation Protection principles aims at protecting the individuals and the environment from such detrimental effects. When correctly implemented, these practices offer guidance to a safer use of ionizing radiation. The international system of Radiation Protection is articulated around three main principles, which are described on the 2007 Recommendations of the *ICRP Publication 103* [2]. When applied to medical exposures, the three Radiation Principles can be summarized as:

1. **Principle of Justification -** All medical practices that imply patient exposures to ionizing radiation must be justified. In diagnostic applications, there must be some guarantee that the necessary exposure of the patient will permit the subsequent image reconstruction of anatomical structures and/or physiological processes, specifically correlated to the patient's diagnostic indications. Even the smallest exposures are potentially harmful, so the radiation risk must always be offset by its benefits [2,25]. In particular, before the patient is exposed to ionizing radiation, other options should be considered: for example, if a MRI or an ultrasound examination can provide an equivalent diagnostic value and if no social, economical or technical factors hinder the realization of those procedures, they should be chosen over an imaging technique that uses ionizing radiation. Furthermore, the imaging technology that

yields the lowest radiation dose should always be selected (for example, a radiography over a CT examination).

2. **Principle of Optimization** - For diagnostic medical procedures, once the exposure to ionizing radiation is justified, each examination should be performed according to the ALARA principle [2,25]. This means that each procedure should be executed in a way that minimizes individual patient dose, as long as the desired outcome – diagnostically valuable information – is achieved. In diagnostic medical examinations, many aspects ought to be considered: greater radiation doses are harmful for the patient, but they usually result in a superior image quality. The image quality/radiation dose binomial must always be considered by the qualified professional that is responsible for the examination, in a way that a compromise between the two is reached. For obvious reasons, the ALARA principle does not apply for therapeutic medical procedures.

3. **Principle of Dose Limitation -** The radiation exposure of patients, professionals and individuals of the public should be restricted to the established dose limits recognized by the responsible authorities on this matter. These limits aim to ensure that no individual is exposed to a radiation risk level that is considered unacceptable, for medical procedures, in "normal circumstances" [2,25].

2.3.2. Dosimetric Units and Quantities

Radiation dosimetry aims at defining a set of units and quantities that allow:

- the characterization of the interaction of ionizing radiation with matter;
- the quantification of the energy transferred from the incoming radiation to the media;
- the quantification of the energy absorbed by the media;
- the characterization of the different types of ionizing radiation in terms of their effects in biological media;
- the assessment and quantification of the biological effects of ionizing radiation in tissues and organs and to infer the associated detrimental aspects of ionizing radiation;
- the establishment of comprehensive operational methods to perform dose measurements.

In this section, some of the most important units, quantities, concepts and weighting factors used for radiation dosimetry purposes, are introduced:

- **Exposure** (X) is defined as the amount of ionization produced in air by a photon radiation field, and its SI unit is given as charge per mass of air: coulomb per kilogram (C/kg) [26]. Exposure is, however, frequently expressed in units of Roentgen (R) and submultiples;
- **Absorbed Dose** (D) is the energy absorbed per unit mass by a given material, from ionizing radiation [27]. It is defined, by ICRP, as expressed in Equation 2.2:

$$D = \frac{d\bar{\varepsilon}}{dm} \qquad \textbf{Equation 2.2}$$

  where $d\bar{\varepsilon}$ is the mean energy delivered to a sample of matter of mass dm [2]. The SI unit for dose is the Gy, which represents the energy per mass unit: joule per kilogram (1 Gy = 1 J/kg) [26];

- The **equivalent dose** (H_T) in an organ or tissue is defined as:

$$H_T = \sum_R w_R \cdot D_{T,R} \qquad \textbf{Equation 2.3}$$

  where w_R is a numerical factor, called the *radiation weighting factor*, based on the type of radiation, R, being used [2]. This value takes into account the efficiency of energy transfer of each type of radiation and the recommended w_R values can be consulted in Table 2.2. The $D_{T,R}$ quantity in the previous equation represents the average absorbed dose in the volume of a specified organ or tissue T. In SI units, H_T is expressed in sieverts (for photons, 1 Sv = 1 Gy), a radiation unit that takes into account the type of radiation used [27];

Table 2.2 – The recommended w_R for most radiation types. Adapted from [2].

Radiation Type	w_R
Photons	1
Electrons	1
Protons	2
Alpha particles and heavy ions	20
Neutrons	(depends on neutron energy)

- The **effective dose** (E) is expressed as a weighted sum of tissue equivalent doses:

$$E = \sum_{T} w_T \cdot H_T \qquad \textbf{Equation 2.4}$$

where w_T is the t*issue weighting factor* (see Table 2.3), which quantifies the tissue radiosensitivity. This weighted sum is performed over all organs and tissues and the w_T values represent the different contributions of each individual organ, or tissue, to the overall biological detriment caused by the radiation exposure. The SI unit for effective dose is also the sievert [2];

Table 2.3 – The recommended w_T. Adapted from [2].

Tissue	$\boldsymbol{w_T}$
Gonads	0,08
Bladder, Oesophagus, Liver, Thyroid	0,04 each
Bone surface, Brain, Salivary glands, Skin	0,10 each
Bone Marrow, Colon, Lung, Stomach, Breast and Remainder Tissues	0,12 each
Total	1

- **Collective Dose** is the product of the average individual effective dose and the number of exposed people, for a given population exposed to a specific radiation source. The SI unit for collective dose is the man·Sv [27];
- Finally, the **committed effective dose**, E(τ), from an incorporated radionuclide is the total dose expected to be delivered within a specified time period (τ), given by [2]:

$$E(\tau) = \sum_{T} w_T \cdot H_T\,(\tau) \qquad \textbf{Equation 2.5}$$

2.3.3. Internal Dosimetry and Biokinetic Models

Living organisms can be either be exposed to external or internal radiation sources: external exposures occur when the radiation source is located outside of the organism, while internal exposures, in humans, take place when radioactive substances are inhaled, ingested or absorbed

through the skin [21]. For the latter type of exposure, the radioactive material can remain inside the body for only a few hours, or for a much longer period – days, weeks or even years, depending on both its radioactive decay and the way it is eliminated (mainly by excreta) by the body [17], within a time interval computed as:

$$T_{ef} = \frac{T_b \times T_{1/2}}{T_b + T_{1/2}} \qquad \textbf{Equation 2.6}$$

In Equation 2.6, T_b, the biological half-life, an organ dependent and characteristic value, represents the required time for the reduction to one-half of the initial value, of the activity initially existing in that organ, and $T_{1/2}$ is the physical half-life, mentioned before. T_{ef} is the total time required for a radioactive substance within the organism to be halved, as a result of both the radioactive transformation and biological elimination [17,21]. The determination of the time-dependent radiation dose in organs and tissues within the body, following the incorporation (by inhalation or ingestion, via skin) of a radioactive substance is extremely complex and requires the development of the so-called biokinetic models, specific of each radionuclide [21].

2.3.4. Protection from External Sources of Radiation – Time, Distance and Shielding

1. **Limiting the duration of the exposure -** The longer the time an individual is exposed, the greater the number of radiation particles interacting with his/her body tissues [28,29] and hence the dose to tissues and organs. Thus, greater detrimental effects can arise as a result of a prolonged exposure, and so the time spent in close proximity to an ionizing radiation source should be no longer than the strictly necessary. This time principle applies to both the patient and the Nuclear Medicine or Radiology technician and also on situations where individual members of the public are potentially exposed.

2. **Increasing the distance between the individual and the radiation source** - Distance is another important factor in the Radiation Protection of workers, patients and members of the public. This protection principle does not apply for Nuclear Medicine patients to whom radioactive tracers have been administered, but it can be implemented to protect other patients in their proximity. As for Radiology patients, except those in Interventional Radiology and Cardiology (fluoroscopy, etc.) this protection method cannot be put into practice, since the patient must

invariably be positioned directly in front of the x-ray primary beam, and so the distance to the radiation source cannot be optimized in a way that reduces exposure. Nevertheless, when this distance principle is indeed applicable, a greater distance between the source and the individual results in an effective of decreasing the dose to which the individual is exposed [29]. The relationship between radiation intensity and distance follows the *inverse square law*, which states that, for point sources (the CT x-ray beam or a radionuclide source may, in some circumstances be approximately assumed to be point-like), the intensity of radiation fields inversely proportional to the square of the distance to the radiation source [30]:

$$I_1 \propto I_2 \cdot \left(\frac{d_2}{d_1}\right)^2 \qquad \textbf{Equation 2.7}$$

where I_1 is the radiation intensity at distance d_1, compared with the intensity (I_2) at some other distance (d_2). This equation indicates that doubling the distance from a radiation source decreases the radiation intensity by a factor of four and, when applied in medical context, it yields a significant reduction in the overall radiation exposure of patients, workers and individuals of the public.

3. **Using Appropriate Shielding** – The use of specific shielding designs for each type of radiation is a practical Radiation Protection method, required by the NCRP, and included in several federal and state regulations. Depending on the type of radiation, different materials (and widths), such as lead or concrete, are used for shielding, in order to decrease the radiation transmission [28]. For example, β particles (used in diagnostic Nuclear Medicine procedures) can be stopped using plastic, but γ-rays (also employed in Nuclear Medicine) and x-rays (used in radiologic examinations) require a more dense shielding material, like lead [30].

2.3.5. Established Dose Limits

In order to meet the aforementioned Dose Limitation Principle, established radiation dose limits, presented in the table below, recommended by the ICRP and legally imposed by European Directives and national legislation, must be respected. This values were last updated in 2007, when new ICRP Recommendations became available in Publication 103 [2].

Table 2.4 – Established Dose Limits for planned exposure situations. Adapted from [2].

Established Dose Limit	Occupational Exposure	Public Exposure
General Dose Limit	~ 20 mSv/year, in 5 years < 50 mSv in a single year	~5 mSv/year < 1 mSv/year in a single year
Lens of the eye	~ 150 mSv/year	~ 15 mSv/year
Skin	~ 500 mSv/year	~ 50 mSv/year
Extremities (hands and feet)	~ 500 mSv/year	NA
Pregnant women	~ 1 mSv to the embryo/fetus (remainder of pregnancy)	NA

Table 2.4 lists the ICRP dose limits for planned exposures, that is, non-accidental exposures to ionizing radiation that can be controlled, like the ones in the context of medical applications. The ICRP defines three types of exposures:

- **Occupational exposure**, which includes "all radiation exposure of workers incurred as a result of their work";
- **Medical exposures**;
- **Public exposure**, which encompasses "all exposures of the public other than occupational exposures and medical exposures of patients" [2].

For dosimetry purposes, the different body regions are usually differentiated: the term "extremities" refers to the arms below the elbow and legs below the hip, and the irradiation of all the remaining regions (head, torso, gonads, arms above the elbow and legs above the knee) are often referred to as whole-body irradiation [24].

Two important remarks need to be clarified: i) the indicated dose values for specific body areas (the lens of the eye, skin and extremities) represent the effective dose limits and ii) general dose limits do not account for differences in the radiosensitivity amongst the human body - for instance, these general values correspond to the measurements of a whole-body dosimeter.

To better understand the magnitude of the dose values presented, one must consider the background radiation levels, which individuals are globally exposed to. The average annual

exposure to unavoidable natural radiation sources (such as cosmic radiation from outer space, or natural radioactive isotopes on Earth) has been estimated to be about 3 mSv [31] for the USA population, although this value can vary greatly, depending on the location. Additionally, radiation exposure from medical applications and other industrial activities can contribute up to another 3 mSv to the individual annual radiation dose [31].

A last note worth mentioning is the constant updating of the dose limit values by the ICRP. In fact, recently - April 21, 2011, the ICRP published a *Statement on Tissue Reactions* [32], which revises the 2007 Recommendations, in the view of recent epidemiological evidence on tissue reaction effects. According to this Statement, this new evidence suggested that the threshold radiation doses for the manifestation of late effects, particularly in the lens of the eye, might be lower than the previously considered values. In short, the ICRP acted on this new information by adjusting the equivalent dose limit for occupational exposure, in planned exposure situations, to: "an equivalent dose limit for the lens of the eye of 20 mSv in a year, averaged over defined periods of 5 years, with no single year exceeding 50 mSv" [32].

3. CT and Nuclear Medicine Imaging Modalities

3.1. Computed Tomography (CT)

3.1.1. An Overview of CT History

Wilhelm Roentgen first discovered ionizing radiation in the form of x-rays in 1895, while performing experiments with cathode rays. Shortly after his discovery, the possible applications of x-rays for medical purposes began to be explored in several countries, including the USA, England and France [33].

In the 1970s, CT was introduced as an innovative x-ray imaging tool. This technology was invented by electrical engineer Godfrey N. Hounsfield of Central Research Laboratories (London) in 1972, along with physicist Allan M. Cormack of Tufts University (Massachusetts), who was simultaneously working on image reconstruction theory [34]. Also in 1972, the first CT head scanner was developed, and the first commercial unit of this prototype was installed in the USA, in 1973 [35,36]. Between 1974 and 1976, CT scanners began to be installed and used in medical institutions. By 1977, several manufacturing companies were marketing more than 30 models of CT scanners [33], and by May 1980, there were more than 1,000 operational CT tomographs in the USA [37].

Spiral CT scanners entered the market in 1989 [38], and the first step towards multi-slice acquisition was the *Elscint TWIN* two-slice CT scanner, introduced in 1993. By 1998, all major CT manufacturers had a multi-slice SCT scanner model and, in 2004, the next-generation versions of those multi-slice CT systems – with 32, 40, and 64 simultaneously acquired slices – were available on the market. 64-slice CT systems are now operational in numerous medical institutions, and yet new tomographs, with more slices acquired simultaneously, are being developed. In 2007, *Phillips* introduced a scanner capable of measuring 256 slices simultaneously, using a RX cone-beam, and *Toshiba* announced a new 320-slice scanner [35].

3.1.2. Applications of CT Imaging

CT is a radiologic, anatomical imaging technique that provides valuable clinical information for the detection and differentiation of several diseases. In fact, CT is the primary diagnostic tool for a wide range of clinical indications, being also used as a complement for other imaging modalities [39]. A CT system produces cross-sectional images of selected regions of the body, which can be used for different diagnostic and therapeutic purposes. The images obtained can help diagnose or rule out different diseases and abnormalities, also being often used as a reference for therapy planning and monitoring [40].

For instance, one of the fields where CT is most widely used is Neuroradiology. It is highly useful in the examination of the brain, being frequently indicated for neurologic examinations such as the evaluation of acute head trauma, suspected intracranial hemorrhage, and vascular lesions. Also in Neurology, CT might be a suitable alternative when MRI is deemed contraindicated [41]. Other advanced applications of CT imaging include the visualization of specific anatomical structures and tissues using CT perfusion, volumetry, angiography, and venography.

3.1.3. Basic Principles of CT Imaging

In CT imaging, anatomic cross-sectional (or "slice") images of body tissues and organs are produced. These images represent the x-ray attenuation properties of the different tissues: the x-ray photons, generated within an x-ray tube, are attenuated in the patient's tissues and organs [42]. The interaction between xray and matter depends on the x -ray photons energy, and matter's thickness and electron density. Thicker and denser materials, such as bone, attenuate more X-rays photons than less dense, thinner tissues like muscle or fat, and these differences in attenuation will result in correspondent contrast variations, in the final image.

Thin x-ray beams scan the desired anatomical region, and this process is repeated for different angle directions [42]. The actual attenuation at each particular location inside the body is then reconstructed from all those attenuation measurements, through sophisticated mathematical algorithms, which reconstruct data information of the x-ray attenuation coefficients determined for the different anatomical structures [43].

The intensity of the x-ray beam before it reaches the body is measured by an x-ray detector, as well as its final intensity, in order to compute the μ values of the different tissues the x-ray beam interacts with [42]. The x-ray detector area is constituted by a radiation-sensitive material (such as cadmium tungstate or gadolinium-oxide), which converts x-rays into visible light. This light interacts with a silicon photodiode and is converted into an electrical current, which is later amplified and converted into a digital signal [35]. The data from the detector array is then reconstructed to obtain images of the internal structures of the body region scanned:

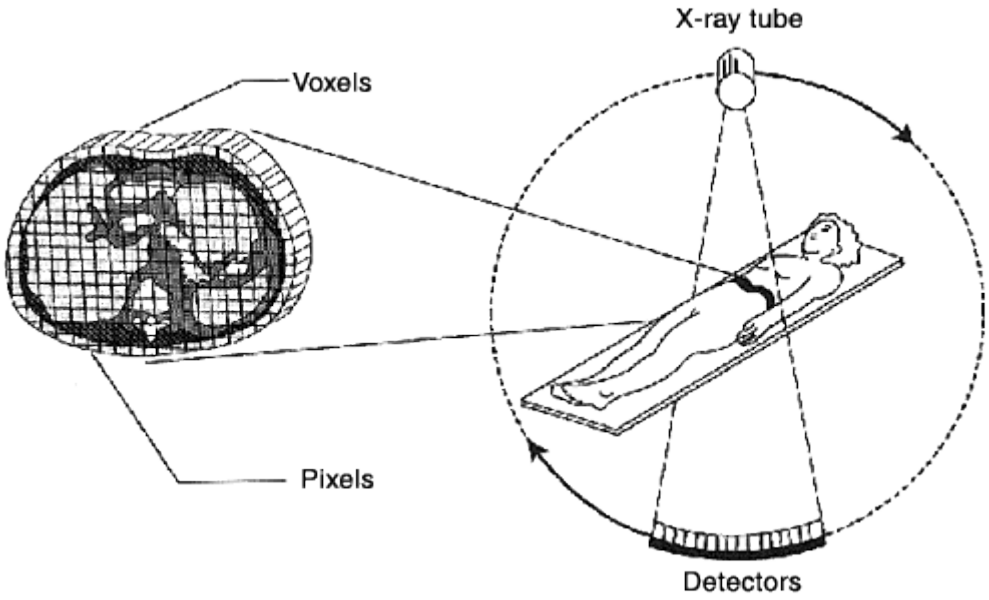


Figure 3.1 – Anatomical structures within the patient's body are reconstructed from the x-ray transmission data. From [44].

3.1.4. The CT Scanner Components

The general structure of a CT equipment can be divided in four principal elements:

1. The *Data Acquisition and Transfer System*, which encompasses the gantry, the patient's table, the PDU and a data transfer unit:

- The **gantry** is a central opening where the patient is moved into during the examination, in which are assembled the **x-ray tube source**, where electrons are generated in a cathode and accelerated towards an anode (the target) producing x-ray photons; the *detector* area, diametrically opposed to the x-ray source in the gantry; a **collimation system**, which determines the slice width; a **filtering system** to remove the low energy component of the x-ray beam; a **refrigerating system** and a **power source** for the x-ray tube and detectors rotation [44]. A sketch of the gantry's design is depicted in Figure 3.2:

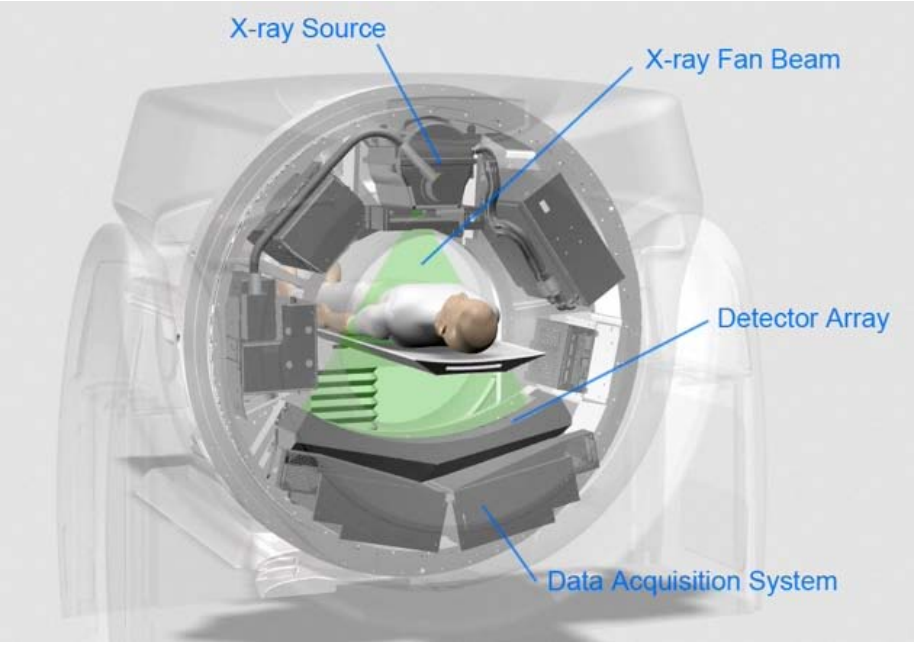


Figure 3.2 – The x-ray tube and the detector array are oppositely placed, inside the gantry. From [45].

- The **table** is where the patient is positioned (lied down), and it moves through the gantry. The patient's table and the gantry constitute CT scanner itself;
- The Power Distribution Unit (**PDU)** supplies power to the gantry, the patient's table and the computers of the Computing System, which is localized in a separate room, as will be explained next. The PDU is a separate, independent unit, generally in the same room as the gantry and table [46];
- In the **data transfer unit**, ADCs (Analog-to-Digital Converters) convert the electrical signal from the detectors in the gantry into a digital signal [47];

2. The **computing system** (or operator's console) is installed in separate room, making it possible for the operator (technician) to control the acquisition process, introducing patient

data and selecting several image acquisition parameters, such as the kV and mA values used [44] (these technical factors will be addressed in section 3.1.5);

3. The **image reconstruction system** receives the x-ray transmission data information from the data transfer unit, in a digital format [44]. This gathered data is then corrected using reconstruction algorithms, and later registered in a CD or a DVD. Generally, all exam data is additionally recorded in the medical institution's PACS;

4. A second **operator's console**, for independent image editing and post-processing is also necessary [44], so it is possible to analyze and review previous exam data, without interfering with the current examinations taking place.

3.1.5. Dosimetric quantities in CT – CTDI, DLP, Effective Dose

In CT examinations, the dose delivered to the patient is strictly related with the final images' quality, both being influenced by several technical factors. Some of these parameters may be adjusted in order to reduce the dose, but the effects on image quality must be considered [48]. Either way, the appropriate adjustment of the parameters listed below is dependent on the purpose of the CT examination to be performed and greater doses to the patient must be justified, in some special cases. These technical factors include:

- The **tube voltage** (in kV) - the voltage supplied to the x-ray tube. It determines how penetrating the x-rays are, and generally ranges between 80 and 140 kV, 120 kV being the preferred value in most cases [49]. A decrease in the x-ray tube voltage reduces the patient's dose, but also increases the resulting image noise [48,50];

- The **tube current** (in mA) - the electrical current provided to the x-ray tube. It determines the number of x-rays produced in the target. The radiation dose is proportional to the product of tube current and total scanning time (in mA·s), which defines the *intensity* of the x-ray beam, if other technical factors are held constant. Therefore, a reduction of the mA·s product results in a lower radiation dose to the patient, but also increases image noise [48,49];

- Several **filtration** techniques - used to remove low-energy x-rays, which increase patient dose without contributing to image quality. The use of filtration is an important technique in order to reduce the dose to the patient;

- **collimation** procedures – which adjust the x-ray beam to the area desired;

- The **pitch** - defined as the "table feed per rotation divided by the total width of the collimated beam" according to the IEC [35]. The pitch reveals whether data acquisition occurs with gaps (pitch > 1) or overlapping (pitch < 1) in the z-axis direction. If pitch equals 1, the patient's table advances the same distance as the collimation width. Usually, the selected pitch value is in between 1 and 2 [44]. A lower pitch means smaller increments in the table movement, and therefore results in a superior spatial resolution along z-axis, but also results in higher patient doses and longer scanning times [33,49].

Two of the most relevant dosimetric units in CT are the Computed Tomography Dose Index (**CTDI**) and the Dose-Length Product (**DLP**), which are indicators of the local dose in the irradiated slice, and the total radiation exposure to the patient, respectively. However, neither the CTDI (in mGy) nor the DLP (in mGy·cm) guarantee a correct estimation of the radiological risk of a CT exposure - the quantity used for this purpose should be the *effective dose* [49], previously introduced in section 2.3.2. The effective dose to the patient can be estimated from the CTDI and the DLP:

- There are several CTDI definitions. The $CTDI_{100}$ represents the integrated dose, along the z-axis, in a length of (usually) 100 mm – the length of the ionization chamber used for measuring the dose profile *D(z)*:

$$CTDI_{100} = \frac{1}{nT} \int_{-50\,mm}^{50\,mm} D(z)dz \qquad \textbf{Equation 3.1}$$

  where *n* is the number of slices, *T* the slice thickness and *D(z)* the dose profile measured in the ionization chamber [51]. Another CTDI definition, the $CTDI_w$, which represents the weighted dose index measured in a dosimetric phantom, is defined as:

$$CTDI_w = \frac{1}{3} CTDI_{100_c} + \frac{2}{3} CTDI_{100_p} \quad \textbf{Equation 3.2}$$

where $CTDI_{100_c}$ and $CTDI_{100_p}$ correspond to the measurements at the centre and periphery of the dosimetric phantom, respectively [52]. One last CTDI definition is the $CTDI_{vol}$, which represents the mean absorbed dose and can be determined using the $CTDI_w$ and the pitch value:

$$CTDI_{vol} = \frac{CTDI_w}{pitch} \quad \textbf{Equation 3.3}$$

- From the $CTDI_{vol}$ value and the scan length, it is possible to calculate the DLP:

$$DLP = CTDI_{vol} \cdot scan\ length \quad \textbf{Equation 3.4}$$

The DLP is usually calculated taking into account the full set of scans of the entire CT examination, in order to provide an estimation of the total radiation dose. Finally, effective doses can be estimated, multiplying the DLP value by a conversion factor, which takes into account the patient's age and the specific anatomical region being imaged:

$$Effective\ Dose\ (E) = conversion\ factor \cdot DLP \quad \textbf{Equation 3.5}$$

3.1.6. Typical Effective Doses in CT Imaging Procedures

Some of the typical effective doses, for several adult CT Procedures, are listed on Table 3.1. Note that these values are merely indicative, as the effective dose for the patient on each CT examination depends on several factors, as mentioned in the section 3.1.5.

Table 3.1 – Typical values of effective doses for adult patients, for different CT examinations. Adapted from [6].

CT Examination	Average Effective Dose (mSv)
Head	**2**

Neck	**3**
Chest	**7**
Abdomen	**8**
Pelvis	**6**
Coronary angiography	**16**

3.2. Nuclear Medicine

3.2.1. An Overview of Nuclear Medicine Imaging History

After radioactivity was first discovered in 1896, by Antoine Henri Becquerel, radioactive substances began to be used in many industrial applications and in Medicine. Radium and polonium were one of the first radioisotopes being studied, by Pierre Curie and Marie Curie [53].

Later, in 1901, Henri Danlos and Eugene Bloch used a radium source for tuberculosis skin lesions' therapy. As for diagnostic purposes, ^{210}Pb and ^{210}Bi radiotracers were first used on animals in 1924 and roughly one year later, ^{214}Bi was used in the study of blood flow rates in humans [53]. In the 1920s, radium was being used in the treatment of cancer and the production of artificial isotopes, such as ^{131}I and ^{60}Co, began in the 1930s. In particular, ^{99m}Tc, nowadays the most commonly used radionuclide in conventional Nuclear Medicine procedures, was discovered by Emilio Segre and Glenn Seaborg around 1937. The first commercial ^{99}Mo-^{99m}Tc generator would only be available in 1964 [54].

In 1953, Gordon Brownell and William Sweet developed a positron detector prototype, on which the diametrically opposite annihilation photons (see section 3.2.5) are detected. However, the standard PET scanner, as we know it, was only introduced several decades later, in November 2000 [55]. As for the Anger (scintillation) camera, used for conventional Nuclear Medicine procedures (as opposed to PET procedures), it was first developed by Hal Anger in 1958 [53].

The initiative of integrating PET imaging with CT technology was first introduced in the 1990s, by David Townsend and Ronald Nutt. The first commercial *Discovery LS* PET/CT scanner (by GE healthcare) included a 4-slice CT tomograph, and it was available in 2001. By 2006, the

majority of Nuclear Medicine centers no longer opted for dedicated PET tomographs, selecting the higher-resolution PET/CT technology instead. As a final point, in the year of 2008, over 2500 PET/CT scanners were operational worldwide [56].

3.2.2. Diagnostic and Therapeutic Applications of Nuclear Medicine

Nuclear Medicine diagnostic procedures are used to reveal functional and metabolic disorders in several organs and tissues, including the brain, thyroid, heart, lungs, kidneys, liver and bone, amongst other structures. A clear advantage of Nuclear Medicine over x-ray techniques, such as CT imaging, is that soft tissues can be imaged with very good results.

For several reasons (to be explained in section 3.2.3), ^{99m}Tc is the most widely used γ-emitting radionuclide. For instance, where Oncology is concerned, this radioisotope is used in the evaluation of metastases, assessment of therapy response and guided radiotherapy planning are the most common indications [54].

MPI (Myocardial Perfusion Imaging) techniques also use ^{99m}Tc or, as an alternative, ^{201}Tl to evaluate coronary artery disease [57]. Various ^{99m}Tc-labeled compounds are used in pulmonary procedures, either to measure perfusion and ventilation or in lung cancer staging.

Moreover, both ^{99m}Tc and ^{67}Ga can be used in brain procedures (for example, in the assessment of blood-brain barrier permeability and cerebral perfusion and metabolic activity), and in the detection of infection and inflammation disorders, using labeled leukocytes that accumulate on the inflammation site [54].

In the assessment of thyroid disease, radio-labeled iodine compounds (^{123}I and ^{131}I, for the most part) are typically used, mainly because iodine is an essential component of thyroid hormones. When it comes to the evaluation of renal function, both iodine and ^{99m}Tc tracers are used.

The most commonly used PET radioisotope is ^{18}F, as other β-emitting radionuclides (such as ^{11}C, ^{13}N and ^{15}O) are too short-lived to be used in medical centers located far from radiotracers production sites [54]. The most important indication for PET examinations is Oncology, where

^{18}F-FDG (a glucose analog, to be addressed later) is often used to detect and stage cancer and to evaluate the response to cancer treatment [58]. Cardiology and Neurology are also fairly common indications for PET imaging [57]: while in Cardiology, ^{18}F-FDG is used to determine the blood flow to myocardial tissue and to evaluate symptoms of coronary artery disease, in Neurology the diagnosis of brain tumors, epilepsy, traumatic brain injury and Alzheimer's disease are amongst the most usual indications for PET [54,58]. Although mammography is the standard method for breast cancer diagnosis, PET procedures are also often used for this indication, particularly in the assessment of breast cancer therapy response [54].

As PET/CT scanners are gradually replacing dedicated PET tomographs, multimodality PET/CT examinations are accordingly used for those same diagnostic indications, indicated above.

Radionuclide metabolic therapy – that is, with radionuclide incorporation – is frequently used in the treatment of some diseases, namely cancer. The incorporated ionizing radiation (a γ or a β emitter) damages targeted cells. ^{131}I is has applications in the treatment of numerous thyroid disorders, either malignant or not. Furthermore, ^{89}Sr, ^{153}Sm and more recently, ^{186}Re are used in palliative therapeutic procedures, for instance in relieving bone metastases pain [57].

3.2.3. Basic Principles of Nuclear Medicine Imaging

γ-emission imaging provides information on the function and metabolism of the different organs and tissues in the body. For this reason, Nuclear Medicine techniques are sometimes classified as an "active" form of imaging [59], given that the patient is actually who constitutes the radiation source (following this line of thinking, anatomical imaging techniques, such as CT, would be "passive" imaging modalities, as the patient is merely irradiated while lying in the scanner table).

All Nuclear Medicine procedures, including both conventional examinations and PET scans, can be separated into three main steps [59]:

1. A radiotracer (a substance that was previously labeled with a γ-emitting radioisotope) is administered (usually, injected) to the patient;

2. The radiotracer (frequently referred to as a *radiopharmaceutical*) is incorporated in the patient's organs and tissues, according to its composition and physiological purpose;

3. The radiopharmaceutical's distribution (*uptake*) amid the patient's anatomical structures is assessed, using gamma detection systems.

For the purposes of Nuclear Medicine imaging, an "ideal" radioisotope comprises the following requirements: an efficient accumulation and retention in the target organ, little or no accumulation in non-target tissues and organs, an half-life of a few hours or few days, low cost, easy preparation (kit formulation) and of course, high specificity for the pathologies being assessed. ^{99m}Tc covers these ideal characteristics: it has a half-life of roughly 6.02 hours and it is chemically versatile (which means it can be used to label innumerous ligands). Additionally, it is produced in a ^{99}Mo-^{99m}Tc generator, which is now available for transportation over long distances (namely, from the production site to medical centers). For these reasons, ^{99m}Tc has become the most widely used radionuclide for a number of diagnostic applications. As for PET radiotracers, the very short half-life of most β^+ emitting isotopes, apart from ^{18}F (half-life of ~110 min), makes it impractical to use them regularly – a cyclotron near the medical center location would be necessary [15,33,54,60].

Table 3.2 lists the most commonly used radioisotopes in Nuclear Medicine and their respective decay mode, energy and half-life:

Table 3.2 – Some of the most frequently used radioisotopes in Nuclear Medicine procedures [15].

Radioisotope	Decay Mode	β or γ Energy (KeV)	$T_{1/2}$
^{11}C	β^+	385,1	20 min
^{13}N	β^+	491,1	10 min
^{15}O	β^+	735,1	124 s
^{18}F	β^+	242,1	109 min
^{67}Ga	EC, γ	93, others	78 h
^{99m}Tc	IC, γ	140	6 h
^{111}In	EC, γ	172, 245	67 h
^{123}I	EC, γ	159	13 h

^{131}**I**	β^-, γ	284,1 (β), 364 (γ)	8 days
^{201}**Tl**	EC, γ	70-80 (EC)	72 h

3.2.4. Conventional Nuclear Medicine – the Gamma Camera

Scintillation cameras are sometimes referred to as *gamma* or *Anger* cameras - the name Anger is related to Harold Anger, who first developed a prototype for scanners in the 1950s. Since that time, these types of cameras have evolved into gradually more modern Nuclear Medicine imaging equipments, partially due to the widespread use and availability of ^{99m}Tc. This radioisotope emits 140 keV γ photons, and the gamma camera is usually optimized for this exact energy level [33].

The external design of a scintillation camera is actually very similar to that of a CT equipment – the patient is placed on a table, which glides through a circular gantry (see Figure 3.3). Additionally, the Anger camera can be divided into three main components: the collimator, the detector unit and the data processing and display unit. A general and brief description of these components is given next, by the order they are encountered by a gamma photon, emitted from the patient's body [15,33].

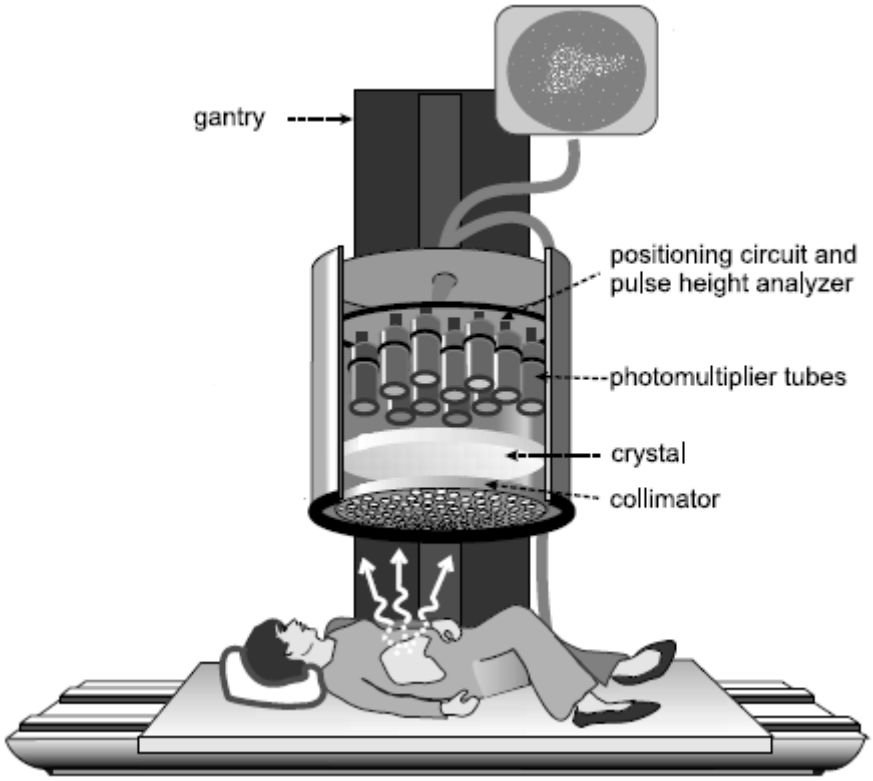


Figure 3.3 – Schematic representation of a gamma camera's gantry (lateral view). Adapted from [15].

In order to create an image of the distribution of the administered radionuclide's activity in the patient's body, the exact location where γ photon absorption occurs, in the camera's detectors, must be precisely correlated with the actual origin of those photons, within the patient's internal structures. This relationship is obtained using a collimator between the detectors and the patient, composed of thousands of small-aligned cylinders (*channels*). The collimator restricts the γ rays' detection: only the photons traveling along the axis of each cylinder are able to reach the crystal; photons emitted in any other direction are absorbed in the lead or tungsten septa existing between the cylinders (see Figure 3.4) [15]. Through this mechanism, γ photons that reach the detectors are correlated with their original location in the patient's body tissues [33].

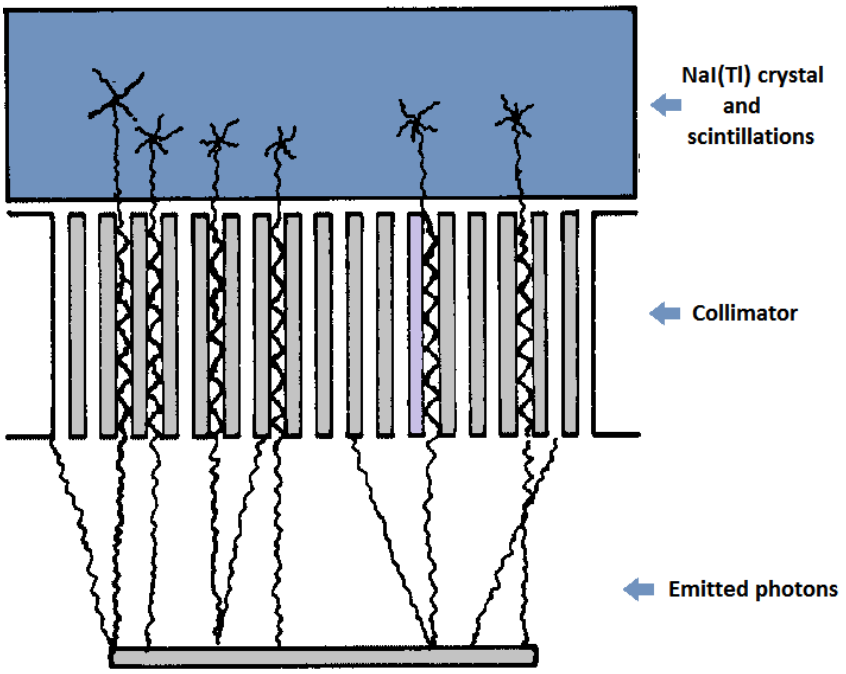


Figure 3.4 – γ photons aligned with the collimator's channels are transmitted to the crystal, whereas obliquely emitted photons are absorbed in the collimator's septa. Adapted from [33].

The detector unit encloses scintillation crystals, PMTs and the associated electronics. NaI (Tl) detectors are used today in nearly all operational scintillation cameras, although other types of crystals (BGO and LSO, for instance) are being explored [33]. The scintillation crystal absorbs gamma photons by means of a photoelectric process. The resulting electron travels through the crystal, colliding with other electrons and thus releasing its energy in the form of visible photons (hence the term "scintillation").

Light photons, originated from a single scintillation at a time, are detected by multiple PMTs, organized in a hexagonal array above the crystal. This detected energy is then measured, and the output signals from all the PMTs are transmitted to a pre-amplifier, used to match the PMT impedance to that of the subsequent circuits. Front-end electronics interface this PMT array to the equipment's computing system, as depicted in Figure 3.5 [42].

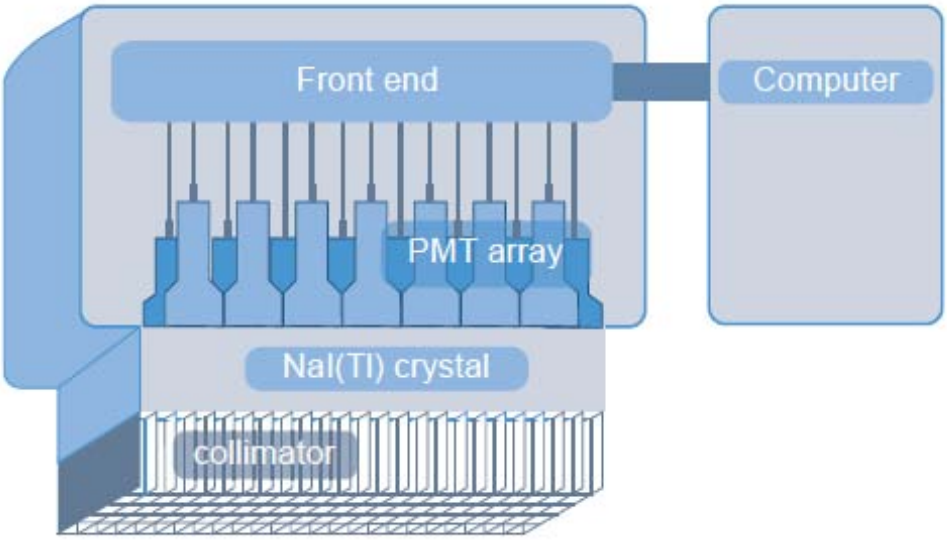


Figure 3.5 – Schematic representation of a gamma camera's design. From [42].

ADCs convert the analog signals from the gamma camera's electronics into a digital signal. The digitized *x* and *y* signals codify the location of different pixels, and the number of counts registered at the correspondent positions will determine these pixels' values. The final reconstructed image, created using the information on the administered radionuclide's distribution, acquired in the gamma camera, may then be digitized, stored and processed [15,33].

3.2.5. The PET Scanner

PET scanners are designed to detect the two 511 keV photons that are emitted when an annihilation event between a positron and an electron occurs:

- When a nucleus is unstable due to a proton excess, a proton is converted into a neutron and a positron (called a positive beta particle), which is a positively charged electron. The released positron, however, is short-lived: after ejected from the atom, it almost instantly reacts with an electron existing in the surrounding matter and both are annihilated, in the form of two 511 keV gamma photons, released in opposite directions [15]:

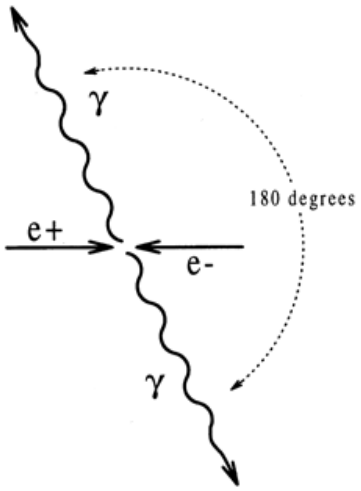


Figure 3.6 – Schematic diagram of a positron-electron annihilation, from [61].

These two annihilation photons are emitted in opposite directions along a straight line (called the LOR) and, if a circular detector array is placed around this annihilation event, both the annihilation photons can be detected, as depicted in the following figure:

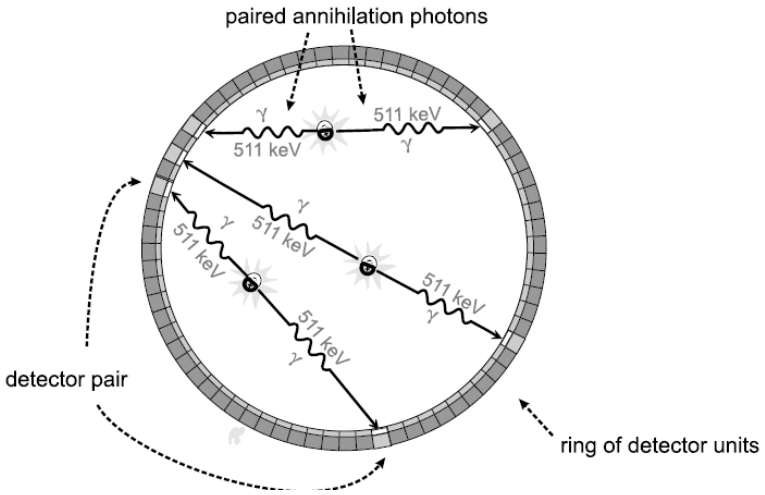


Figure 3.7 – Examples of annihilation events, being detected by a circular detector array. From [15].

In a PET tomograph, the detector array is placed inside the gantry, in this circular fashion. The patient (to whom has been administered a positron-emitting radiopharmaceutical) is placed inside this gantry and, during the data acquisition process, the detectors continuously register information (quantity and location) on the detected annihilation events. Nowadays, these

detectors are usually composed of BGO, LSO or GSO scintillation crystals which, due to their high density and atomic number , are particularly sensitive in detecting photons [15].

These crystals convert the coincident annihilation photons into light, which is then directed to a set of PMTs (highly sensitive light detectors). The exact location of each annihilation event site is determined by measuring the light detected by the PMTs. After data acquisition is completed, the equipment's computing system uses reconstruction algorithms (filtered back-projection, for instance) to the map the annihilation events with high efficiency. The final reconstructed images depict the concentration of the administered radionuclide within the body regions scanned [58].

There are several aspects worth mentioning, concerning the PET image acquisition process. The simultaneous detection of two photons, in two opposing detector units, is referred to as a *coincidence*. If those two photons were originated in the same annihilation, a *true coincidence* event is said to have occurred [61]. However, often photons are scattered (*scatter* coincidence), or absorbed, before leaving the patient's body. This *attenuation* (loss of true coincidence events) occurs every time that a photon is somehow stopped, or deflected, and therefore never reaches a detector unit.

Attenuation correction is therefore necessary after data acquisition, because the two diametrically opposed emitted photons of one annihilation are absorbed and scattered by the patient's body structures, which results in a non-uniform attenuation of the measured signal. If attenuation correction is not performed, a few image artifacts may occur, for example, an apparent higher activity is shown at body surface edges (due to a relatively less attenuation at the surface, in comparison with deeper internal structures) and areas of intense activity appear distorted in the final image [62].

Furthermore, if one photon is scattered, it might reach another detector, which leads to an increased noise level and, ultimately, to an erroneous quantification of activity concentrations. Additionally, photons emitted simultaneously from different annihilation events (*random coincidence* events) may reach the detectors at the same time and, as a result, they are mistakenly registered as resulting from the same annihilation. Both random and scatter events

contribute to an amplification of event counts, and therefore result in a decreased image contrast [59].

3.2.6. Dose in Nuclear Medicine

In Nuclear Medicine, radiotracers can be administered intravenously (mostly), orally or by inhalation but, either way, different amounts of activity will be deposited, and accumulated, in different organs and tissues (and not exclusively in the target organ). If we were to consider a homogeneous mass of tissue, where a radionuclide is uniformly distributed, the dose rate to that same tissue would depends on three factors:

1. The concentration of the nuclide in the tissue *(*in Bq/kg);

2. The average energy released per disintegration (in MeV);

3. The fraction (let us call it φ) of that released energy that is actually absorbed in the tissue.

The MIRD (Medical International Radiation Dose) Committee has developed a simple approach to compute the absorbed dose in specific organs, in which φ, divided by the estimated mass of the organ, is considered to have a specific value for each radionuclide, source organ (where the nuclide is accumulated) and target organ (for which the absorbed dose is to be determined). This value is often referred to as *S* - the mean absorbed dose per unit cumulative activity, available in standard tables [15]. The absorbed dose in the target organ may be computed as expressed in Equation 3.6 [15,33]:

$$D = \widetilde{\mathrm{A}} \cdot \mathrm{S} \qquad \textbf{Equation 3.6}$$

where Ã is the accumulated activity in the source organ, obtained from biokinetic data (standard biokinetic models are now being developed by the ICRP, to assess activity "flow" through the complex physiological compartments existing within the human body). Ultimately, the total dose to a particular target organ would have to include the contributions of all the identified source organs [15,33].

Although undoubtedly relevant, these complex calculations are impracticable to perform in a daily basis, whenever the administration of radionuclides to a patient is concerned. Usually,

the absorbed dose or the effective dose for the patient are never estimated – the administered activity is the one parameter taken into consideration when implementing the second and third principles of Radiation Protection (optimization and dose limitation). For instance, the activity to be administered is mostly calculated, in adults considering patient's weight and, in some cases, predefined suggested dosages [63] and standard maximum levels of activity, per examination [64,65]. For pediatric patients, the EANM (European Association of Nuclear Medicine) has published a Dosage Card [66], on which the child's body weight is also the determining factor, but subject to a minimum acceptable amount of activity.

Finally, in Nuclear Medicine imaging, the radiation dose for individuals near the injected patient is also something to considerer, since the patient becomes a radiation source from the moment he is administered the radiotracer. For instance, a Nuclear Medicine technologist performing a PET study usually is exposed to a considerably higher dose, when compared that he/she would be exposed in a conventional Nuclear Medicine examination [15]. Dose to the extremities may also be considerable when radioactive materials are handled, namely associated to the syringe manipulation at the different phases of the medical procedure.

3.2.7. Estimates of Effective Dose in Nuclear Medicine Imaging Procedures

According to a special report published in *Radiology*, in 2008 [6], Nuclear Medicine effective doses for the patient can vary between 0.3 and 20 mSv:

Table 3.3 – Adult effective doses from some Nuclear Medicine examinations. Adapted from [6].

Nuclear Medicine Examination	Effective Dose (mSv)	Administered Activity (MBq)
Brain (^{99m}Tc-HMPAO)	6.9	740
Thyroid scan (sodium ^{123}I)	1.9	25
Cardiac stress-rest test (^{201}Tl chloride)	40.7	185
Renal (^{99m}Tc-MAG3)	2.6	370
Bone (^{99m}TC-MDP)	6.3	1110
Tumor (^{18}F-FDG)	14.1	740

It is also important to refer the estimates of effective doses for Nuclear Medicine technicians and individual members of the public in close proximity to a "radioactive" patient. A 2007 study [67], published in the *Brazilian Archives of Biology and Technology* Journal, evaluated the radiation dose delivered to technologists manipulating ^{18}F-FDG tracers, in two French Nuclear Medicine facilities. The average monthly whole-body dose absorbed by the technologists was estimated to be about 0.19 mSv for one of the facilities, and 0.33 mSv for the other (the dissimilar results are presumed to be related to differences in the Radiation Protection conditions of each Nuclear Medicine department). Another older study [68], in 1999, compared various dose-rate estimations of Nuclear Medicine technologists, nurses and individual members of the public, using the available data from several work groups. For instance, this study mentions a 1990 assessment [69] of average doses to individuals located at different distances from an injected patient, in a Nuclear Medicine facility's waiting room. In this study, the average dose to other patients in the room was estimated to be around 0.2 mSv, and the average dose to accompanying relatives, about 2.0 mSv.

3.3. Hybrid Systems – PET/CT

3.3.1. Hybrid Systems Advantages and Applications

PET's theoretical limited spatial resolution of about 5-7 mm [62] makes it difficult to determine, in some specific cases, the precise anatomical location of the high metabolic activity regions identified. The correlation of CT's excellent resolution with PET functional images would be ideal in these situations, and this is the main advantage that hybrid modalities, such as PET/CT[2], offer to Nuclear Medicine imaging [55].

The main advantage of hybrid technologies is, therefore, the good superimposition of a metabolic functional image (in the case of this work, PET) with a high-resolution anatomical image (CT), which is particularly relevant when an accurate localization of small structures is

[2] As the only multimodality imaging technique being studied in this work is PET/CT, the next few sections will focus mainly on this hybrid technology.

needed. PET and CT images can be acquired separately, and if they are not very distant in time, a posterior fusion of images can provide a good correlation of anatomical structures between the two sets of information data. However, fusion methodologies do not always provide good results, because there are unavoidable discrepancies in the patient's internal structures positioning, simply because both examinations are not executed at the same time, and in the same scanner table [55].

The PET/CT modality comprises yet another advantage: the image acquisition process is significantly faster – in fact, a PET examination, which can usually take up to one hour, can be shortened to a 30 minutes- duration procedure, just by merely adding the CT acquisition (in a combined PET/CT examination) [55]. Patients obviously benefit from this reduction of the total scanning time, which also reduces the chances of motion artifacts to occur. Moreover, the higher patient output optimizes the use of ^{18}F-FDG doses (FDG is usually provided by an external production site, and hence Nuclear Medicine institutions need to manage the remaining ^{18}F activity) [62].

For the reasons mentioned above, hybrid PET/CT equipments are gradually substituting PET scanners in use. In fact, it has been anticipated that PET/CT procedures will eventually replace PET examinations and become the routine procedure in, for instance, abdomen and pelvic examinations [70].

The most common indications for PET-CT examinations are lung cancer and lymphoma [**62**]. Other applications of this hybrid imaging technique include the detection of recurrent or residual brain tumor after therapy, the identification of metastases in head and neck cancer, as well as the diagnosis of many other types of cancer, infectious and inflammatory diseases and Cardiology and Neurology indications [10,71]. Additionally, some studies indicate that PET/CT provides a higher resolution in the delimiting of tumor volumes in radiation therapy planning, in comparison with the PET technique alone [62].

3.3.2. The PET/CT Scanner

A PET/CT scanner can be divided in three major components: the PET scanner, the CT scanner, and a single patient bed [72]. Both the PET and the CT tomographs are included, and aligned, in the same gantry. The CT scanner is usually located in the front part of their common gantry [62,73], as depicted in Figure 3.8. In the majority of the available commercial PET/CT equipments, the two tomographs are completely independent from one another, with separate detectors and electronics [72].

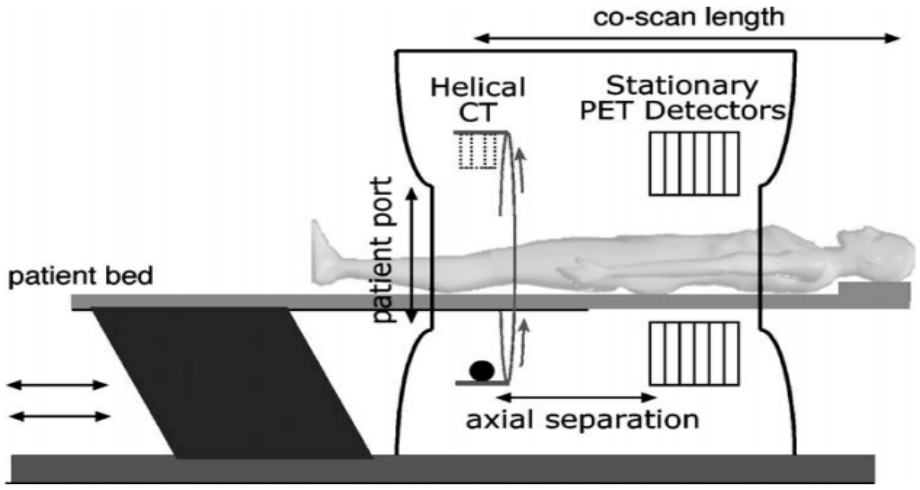


Figure 3.8 – Schematic representation of a PET/CT scanner. From [74].

3.3.3. The PET/CT Imaging Procedure

In PET/CT imaging, a whole-body CT scout scan (of approximately 2 to 10 seconds) usually precedes the actual CT (30 seconds to 2 minutes) and PET (5 to 45 minutes) acquisitions[3] - executed by this order [72]. The scout scan is used as an anatomical reference for the subsequent scans – the regions to be scanned are defined in this step. The CT scan is usually performed at 100–140 kV (with varying tube current values), and after it is completed the bed advances in the direction of the PET scanner, until the patient is positioned within its FOV [73].

[3] These combined scanners can also be used for dedicated PET or dedicated CT examinations, but it is not very common given that the main benefit of a multimodality imaging equipment is the possibility of acquiring *both* CT and PET diagnostic information data, in a single examination.

After the full acquisition is completed, CT data is used for the attenuation correction of PET data. An attenuation map is constructed, in which anatomical density differences in the patient's body structures are used to correct the absorption of the annihilation photons [62,75]. Finally, the CT and PET images are overlaid (fused). A schematic diagram of a standard PET/CT acquisition can be observed in Figure 3.9:

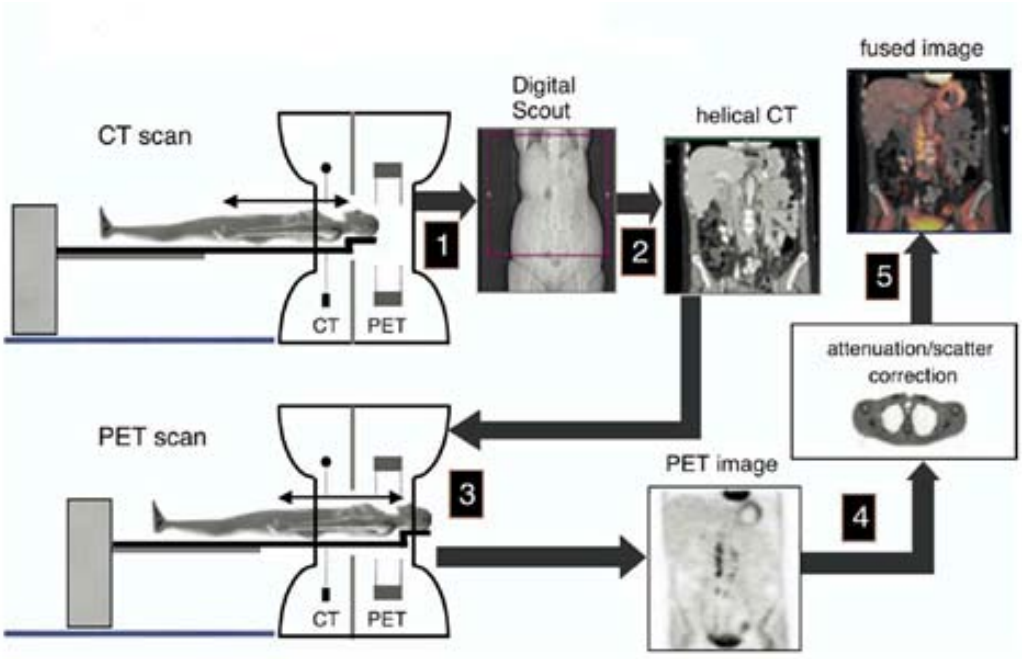


Figure 3.9 – A standard PET/CT acquisition: a CT scout scan is acquired (1). Patients undergo the CT portion of the procedure (2), followed by the PET acquisition (3). After attenuation correction (4), the final co-registered image is obtained (5). From [75].

3.3.4. Radiation Dose in PET/CT

While the radiation exposure from the administered radiopharmaceutical (usually ^{18}F-FDG), relative to the "PET component" of a PET/CT examination, results in an internal irradiation of the patient, he/she is also exposed to an external source of radiation (the x-ray tube), from the CT acquisition. Therefore, PET/CT examinations result in an increased radiation dose for the patient, given that, in the end, he/she actually undergoes two different medical examinations involving ionizing radiation. For this reason, multimodality examinations are normally executed using low dose CT scans (with lower kV and/or mA values) [71], because these are mostly used

as an anatomical reference for the PET acquisition (except when a diagnostic CT scan is also necessary). In comparison with a CT scan, the effective doses patients are exposed to from a PET scan are very low, depending on the injected activity. Since this activity is administered considering patient weight, it would be the same if a smaller part of the patient's body were to be imaged. Hence, the administered activity usually cannot be largely reduced, and so the easiest way to decrease radiation doses from PET/CT scans is by optimizing and adjusting the acquisition CT technical factors (see section 3.1.5) to each patient.

3.3.5. Estimates of Effective Dose in PET/CT Imaging Procedures

In a combined PET/CT procedure, both the internal exposure from the administered radiopharmaceutical and the external exposure from CT contribute to the total effective dose of the patient. Accordingly, the estimates of both CT and PET effective doses, if available, can be simply added up, in order to calculate the total effective dose for the patient, during one single PET/CT examination.

For instance, in a recent study in Thailand [76], the effective doses of 35 oncology patients who underwent 18F-FDG whole-body PET/CT examinations were estimated: the external doses, from the CT scans, were calculated through Monte Carlo simulation techniques, and the patients' internal effective doses were estimated using the mean absorbed dose of 13 target organs. In average, the whole-body effective dose from those multimodality examinations was 18.85 ± 3.20 mSv, ranging from 13.23 to 26.34 mSv.

4. CT, Nuclear Medicine and PET/CT Dose Optimization Study (Results)

In order to better understand the Portuguese reality in what concerns the implementation of Optimization and Radiation Protection practices in CT, conventional Nuclear Medicine and PET/CT procedures, nine medical institutions were contacted, and their Radiology and Nuclear Medicine departments were visited.

While visiting the different Nuclear Medicine departments, it was possible to observe and to get acquainted with:

- Several Nuclear Medicine and PET/CT examinations taking place, including both the radiopharmaceutical administration to the patient and the image acquisition process.
- The radiopharmaceuticals' labeling and Quality Control procedures and
- The periodic maintenance of two PET/CT equipments performed by the manufacturer's specialized technicians.

Additionally a number of questions focusing on the operational aspects of the implementation of radiation protection principles, namely the Optimization principle, were kindly clarified by the Nuclear Medicine department's professionals, particularly technicians and physicists. The gathered information was subsequently organized in a written questionnaire-like form, which can be consulted in the Appendices section of this thesis. This questionnaire helped to structure all the questions and respective answers for the visited institutions, and better analyze the collected information.

Besides assembling information on the general features of each Nuclear Medicine institution, such as its functional organization, imaging equipments, performed examinations and radionuclides used, special attention was given to the implemented practices on the different medical facilities, concerning the patient preparation for the examination and Dose Optimization/Radiation Protection procedures for the patient, workers and members of the public.

A different approach was adopted during the visits to the Radiology departments. Available data (both technical parameters such as kV, mAs, etc. and dosimetric-related data such as CTDI) concerning the CT examinations performed were collected and analyzed, with the ultimate goal of assessing patient effective doses. Finally, dose measurements were performed on the CT units of the visited institutions, using appropriate phantom and radiation detection equipments.

The analysis of both the CT examinations data and of the phantom measurements´ data was used to formulate Optimization and Radiation Protection recommendations. The implementation of the Optimization principle leads to dose reduction and as such, the expression "Dose Optimization" will very often be used in the sequence.

For the sake of keeping the confidentiality of the hospitals, professionals, patients and of the data kindly provided and analysed, the hospital names will not be used; instead, they will be named "Hospital A", "Hospital B", "Hospital C", "Hospital D", "Hospital E" and "Hospital F" (Nuclear Medicine services) and "Hospital H1" and "Hospital H2" (Radiology departments).

4.1. Dose Optimization in Nuclear Medicine and PET/CT

4.1.1. Visited Nuclear Medicine facilities - general features

Six Nuclear Medicine departments (integrated in both public and private hospitals and institutions) were visited in Lisbon, Coimbra and Almada. One of the visited institutions is a dedicated Nuclear Medicine center, whereas the other five are integrated in a multidisciplinary hospital.

In one of the visited hospitals, the Nuclear Medicine department has two therapeutic rooms, for inpatients that undergo therapy-using radiopharmaceuticals. The majority of the other Nuclear Medicine departments also offer the possibility of radiopharmaceutical therapy, but only for ambulatory patients. As for diagnostic procedures, only one of the six facilities performs exclusively conventional Nuclear Medicine examinations. The other five institutions own a PET/CT unit, and therefore offer the possibility of multimodality examinations. Additionally, two of the visited institutions comprise a bone densitometer, and one of them owns a PEM (Positron Emission Mammography) prototype, exclusively used for academic research purposes. The graphic of Figure 4.1 depicts the number of equipments of each type, for the visited institutions:

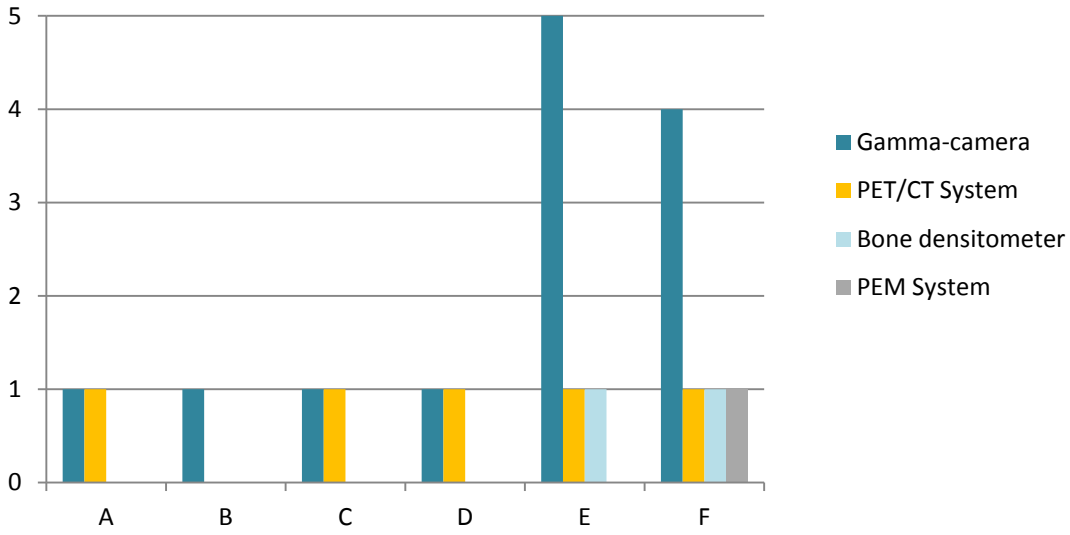


Figure 4.1 – Number and type of equipments existing in the visited Nuclear Medicine Services (identified with the letters A - F).

All PET/CT systems and gamma-cameras were installed by GE Healthcare, Philips Healthcare, or Siemens Healthcare. As expected, Oncology, Cardiology, Osteoarticular Diseases (including Rheumatology), Nephrology and Neurology are the most common Medicine specialties for which Nuclear Medicine examinations are prescribed. In particular, one of the visited departments kindly provided statistical data on the relative percentage of the different Medicine specialties for which conventional Nuclear Medicine is used. Figure 4.2 illustrates the relative frequency of the medical examinations performed during the year of 2010[4] (data from only one of the six institutions):

[4] This information is hereby presented as merely an example and it is not to be generalized, as it is not, in any way, representative of the national distribution of the performed Nuclear Medicine examinations for the different Medicine specialties.

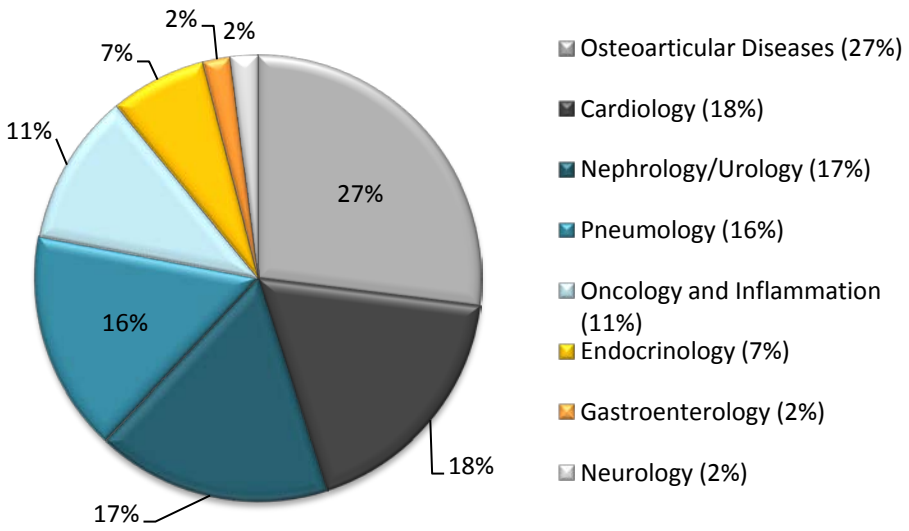


Figure 4.2 – Relative frequency of the different medical specialties for which conventional Nuclear Medicine examinations were prescribed, during the year of 2010, in one of the visited institutions.

The professionals contacted in each Nuclear Medicine unit included the department director, specialized technologists, physicists and others, such as medical physicians, nurses and trainee students. On all institutions, when asked on the number of daily performed examinations, professionals reported the number of conventional Nuclear Medicine examinations to be around 10-20 studies, and PET/CT examinations (when applied), to range from 5 to 10, approximately. The percentage of pediatric examinations is relatively low, ranging from 5 to 10% in most of the visited institutions.

Concerning gamma-emitting tracers, the visited Nuclear Medicine departments predominantly use ^{99m}Tc and, in a less regular basis, ^{67}Ga and ^{123}I. In some institutions, other radionuclides, such as ^{111}In or ^{201}Tl, were also mentioned, and ^{131}I is sometimes used for radiopharmaceutical therapy, in particular.

^{18}F-FDG is the most commonly used tracer for PET/CT examinations. In some facilities, other ^{18}F-labelled compounds are sporadically used but, apart from ^{18}F, no other beta-emitting radionuclides are used.

As for the source of the radioactive tracers used, the Nuclear Medicine facilities regularly order their ^{90}Mo-^{99m}Tc generators and other radionuclides (or already labeled radiopharmaceuticals) according

to the number of scheduled examinations, from different international production sites – in one of the visited institutions, the contacted professionals reported their radionuclides to be supplied by Spanish and English sources, for example. As an exception, one of the visited institutions encompasses an in-house cyclotron for PET tracers.

Finally, a few considerations on the general structure and layout of the different Nuclear Medicine departments, specially related the Radiation Protection of workers, patients and members-of-the-public, are worth mentioning:

- In the majority of the visited institutions, the different functional areas and rooms within the Nuclear Medicine department are grouped by increasing level of activity (from the perspective of someone who enters de Nuclear Medicine department). The ideal layout of a Nuclear Medicine is displayed in Figure 4.3:

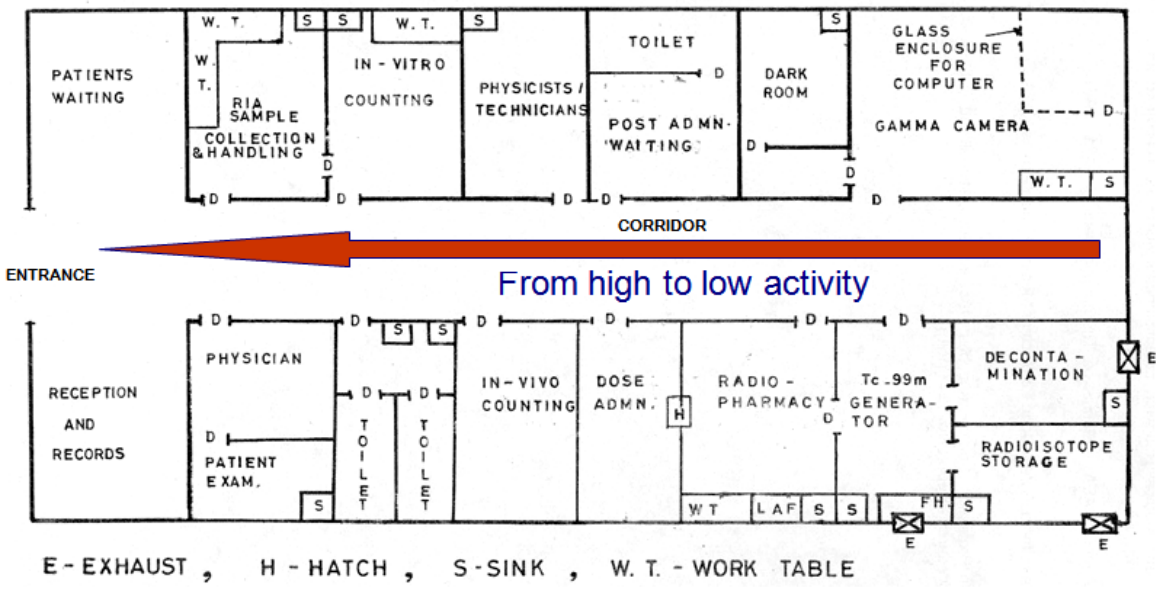


Figure 4.3 – Layout of a Nuclear Medicine department. Adapted from [77].

- In most of the institutions, area radiation levels are monitored, particularly in active or "hot" rooms and areas;
- Some (but not all) of the visited institutions include an exclusive toilet room for injected patients, with special Radiation Protection features (namely, with drain pipes leading to a decay tank where biological radioactive waste is retained for a predetermined amount of time, after which its activity is considered small enough for it to be released on the building's main sewer).

4.1.2. Dose Optimization Strategies

4.1.2.1. Patient Preparation

Once a radiopharmaceutical has been administered to a patient, he or she becomes a mobile source of radiation for other patients, workers and members of the public accompanying patients, comforters and carers. Therefore, since each patient has to wait for the administered radiopharmaceutical to accumulate within the different organs and tissues, before scanning is initiated (about 30-60 min in PET, and up to 4 hours in conventional Nuclear Medicine procedures – according to the professionals contacted within the visited medical institutions), the recommendations given to the patient during this waiting time are an important Optimization issue, concerning the Dose Optimization of the patient the reduction of the exposure of the other individuals (workers and members of the public, comforters and carers). Amongst the visited institutions, these recommendations include:

- In general, for both conventional Nuclear Medicine and PET/CT examinations, the injected patients are recommended to urinate frequently and be well hydrated, while they wait for their examination;

- In conventional Nuclear Medicine procedures, patients are told to either remain in an injected patients' waiting room, or to leave the institution for a while, and then return for the image acquisition process;

- In PET/CT procedures, the injected patients must remain in an isolated rest area, while they wait for the PET examination (the average ^{18}F-FDG uptake period varies between 30-60 minutes, depending on the examination to be performed);

- Dose Optimization in children is achieved through scheduling all pediatric examinations for the same day or days of the week, so that children exposure from injected adult patients is minimized. For logistic reasons, other groupings of patients (by examination, for instance) are organized for different days of the week.

In all the visited institutions, radiopharmaceutical administration (mostly through intravenous injection and, in some specific examinations, by inhalation or ingestion) is based on patient weight and maximum established limits.

The administration of a pharmaceutical (whether radioactive or not) to a patient implies the assessment of some important biological parameters. For example, blood glucose levels are always checked before ^{18}F-FDG administration, and inclusively some of the contacted Nuclear Medicine technicians pointed out the importance of adapting protocols to diabetic patients. In addition, other parameters, specifically related to the examination to be performed, need to be assessed – for example, in cardiac stress test examinations, blood pressure and the electrical activity of the heart are monitored. Professionals also reported additional dietary requirements to be necessary for each examination in specific. In particular, no caffeine (or other stimulant substances) and a high-fat meal (to be ingested at the institution) are common pre-requisites for cardiac examinations, whereas PET studies require fasting and no physical stress in the past 24 hours. Due to possible interaction of the administered radiopharmaceutical with other pharmaceuticals the patient is taking, some examinations may also need specific drug suspension. Moreover, other drugs (in addition to the radiopharmaceutical) are frequently administered:

- Adenosine or similar substances, which induce cardiac stress, in cardiac stress test examinations;
- Anesthesia, particularly in restless pediatric patients (only when it is strictly necessary – this is a very rare procedure);
- Muscle relaxant (5 to 10 mg) in PET procedures, in order to reduce ^{18}F-FDG uptake by the muscle;
- *Lasix* or other diuretic drugs;
- Other specific pharmaceuticals, depending on the situation.

Nevertheless, the institution's medical physician or, occasionally, a Nuclear Medicine technician always assesses the patient's medical history, prior to the radiopharmaceutical administration.

4.1.2.2. Protective Measures for Workers

As a rule, the workers who directly handle radiopharmaceuticals need to be controlled for extremities' dose. In all of the visited Nuclear Medicine Services, technologists use a ring dosimeter

(see Figure 4.4). In all of the visited departments, whole-body dosimeters (see Figure 4.4) are used by all the professionals who have access to controlled and supervised areas within the Nuclear Medicine department.

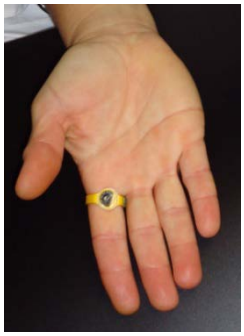
a)  b) 

Figure 4.4 – a) Whole-body dosimeter and b) ring dosimeter [pictures taken in one of the visited Nuclear Medicine departments].

When asked whether dose limits are ever exceeded, technologists reported that it seldom happened. However, professionals generally are not aware of the daily activities they manipulate, and the subsequent radiation doses they are exposed to - apart from their individual dosimetry records. One of the visited institutions provided data on the individual dosimetry records of its employees, as well as estimates of the dose received from performing different tasks, where radiopharmaceutical handling is involved. Since this information is confidential, all data was collected provided that workers will not be identified. A brief analysis of the gathered data revealed that:

- for 8 workers, controlled over a one-year period, both the average equivalent dose, at a depth of 10 mm (Hp(10)) and the skin equivalent dose, at a depth of 0,07 mm (Hp(0,07)) of category A[5] workers were 0,24 mSv (mean value). A null value (0,00 mSv) was observed for both the Hp(10) and the Hp(0,07) of one category B[6] worker;
- for 21 category A workers, also controlled over a period of one year, the average Hp(10) value was 1,08 mSv and the average Hp(0,07) value was 0,18 mSv;

[5] Professionals who directly handle radiopharmaceuticals are normally classified as category A workers [88].

[6] Category B professionals have access to controlled and supervised areas but are not liable to receive radiation doses (in excess of 6 mSv/year) hat would have them classified as category A workers [88].

- tasks involving the proximity to an injected patient contribute the most to the technologist annual dose, when the manipulation of ^{99m}Tc-labelled radiopharmaceuticals is concerned, as shown in Table 4.1:

Table 4.1 – Mean Effective Dose per task performed, in ^{99m}Tc procedures executed in one of the visited institutions.

Task	**E (µSv)** ***per task***		**Daily Freq.** ***per worker***		**E (µSv)** ***per worker***	**Annual E (µSv)** ***200 days a year***
Eluation of ^{99}Mo/^{99m}Tc generator	0,006	X	1	=	0,006	1,2
Kit Preparation	0,024	X	3	=	0,072	14,4
Radiopharmaceutical Administration	0,1	X	10	=	1	200
Patient Accompaniment	0,27	X	10	=	2,7	540

Given the results above, and also as confirmed by most technologists in the visited institutions, the radiopharmaceutical administration to the patient is one of the tasks from which result exposure to higher (but very moderate values) doses to the workers, not only due to the close proximity to the patient being injected, but specially because contaminations can occur and syringe protections are not always used, allegedly because they are “too heavy” and “hamper the administration process, especially in restless or very small children, and oncology patients”.

The implementation of this administration process is also different in the several visited institutions: in two of them, it is a nurse who performs the administration, whilst in the other four units this task is exclusively executed by Nuclear Medicine technologists.

The most commonly implemented Radiation Protection and Dose Optimization practices, regarding the workers, include:

- A system of rotating shifts preventing the same worker to perform always the same type of procedures (although, in a few cases, complex tasks are preferentially attributed to experienced professionals);
- All the necessary instructions are given to the patient before he/she is injected, in order to reduce the time that workers are exposed to "radioactive" patients;

- Tongs are used to increase the distance to radioactive sources, such as vials or syringes, when they are manipulated:

Figure 4.5 – Tongs, used to increase the distance to a radioactive source. From [78].

- Lead and tungsten protections and vials are used during radiopharmaceuticals' preparation and administration:

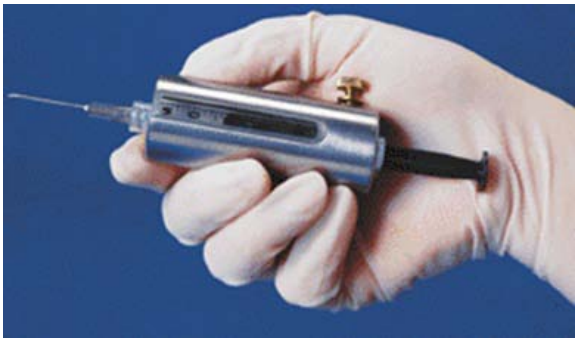


Figure 4.6 – Lead protection for a radiopharmaceutical's syringe. From [78].

- A lead glass window in the scanner room protects the professionals during the image acquisition process;
- Other mobile shields are used when transporting and storing radioactive sources.

Special attention must be given to pregnant workers – since the moment pregnancy is first know, precautions must be taken in order to limit fetus exposure until the remainder of the pregnancy. Radiation Protection measures for the unborn child include the initiation of fetus dosimetry, by means of a direct-reading dosimeter to be used on the abdomen by the pregnant worker, who performs "radiation-safe" functions only (where exposure from the patient and other radioactive sources is virtually null), such as image processing or any type of "desk work".

Apprentices and students may have access to controlled areas for extended periods of time (days, weeks or months), and so dosimetry is recommended in those cases – either using a direct-reading dosimeter, provided by the Nuclear Medicine department, or an individual dosimeter (which is usually attributed to the student by his/her own institution).

Finally, eventual accidents and contaminations are properly registered and recorded in all of the visited institutions, although, in general, contamination monitoring and assessment is only implemented whenever there is a real possibility or suspicion of contamination (and not regularly, as a good practice).

4.1.2.3. Members-of-the-Public Dose Optimization

Considering the exposure of members of the public by the patient (radiation source), two different situations must be taken into account:

1. The exposure of family members and others members of the general population at home and public locations, after the injected patient is discharged from the institution. The most common practice to minimize this exposure is to warn the patient, and give him/her instructions on how to proceed:

    - Limit the time spent in close proximity to pregnant women and small children;
    - Limit the time spent in small, crowded places - such as public transportation.

The decision to discharge the patient also has an impact on the overall population exposure, particularly when treatment with radionuclides – requiring internment of the patient – is concerned. In ambulatory regimen and in diagnostic procedures, the patient is always discharged after the examination is complete, since the administered activities are always below 740 MBq (20 mCi), the cutoff value above which internment is necessary [79], according to the contacted professionals.

2. The exposure of family members who accompany the patient during his/her examination, within the institution. This exposure is specially amplified in pediatric examinations, when the parents' presence is often necessary, in order to sooth the child. Dose Optimization is achieved in those cases by means of allowing only one of the parents into the administration and scanning rooms, and only when it is absolutely necessary.

Injected patients waiting for the examination must be isolated from members of the public and other patients, inside an appropriate waiting room - which exists in most of the visited hospitals. Another common practice that minimizes exposure from injected patients, within the institution, is to instruct the patient to leave the institution after he/she has been administered the radiopharmaceutical, and then return for the image acquisition process, in conventional Nuclear Medicine examinations (PET patients have exclusive, isolated waiting rooms). As for pediatric exposure, exclusive areas for children do not exist in most of the institutions and it is a common procedure in all of the visited hospitals, to schedule all pediatric examinations for the same day of the week.

Either way, the prospective doses for members of the public from patients, while inside a Nuclear Medicine institution, are very low and for this reason, a dosimetric control is never performed.

4.2. Dose Optimization in CT

4.2.1. The CT component of PET/CT Examinations

There were five PET/CT equipments in the six visited Nuclear Medicine institutions and, according to the professionals contacted, the CT technology is always used for attenuation correction and anatomical reference for the PET acquisition, and therefore usually it isn't necessary a high-resolution CT equipment (none of the equipments allowed for more than 16 simultaneously acquired slices). Also, the CT technical factors used generally involve a low irradiation of the patient, comparing to a standard isolated CT examination – as an example, in one of the visited institutions, a value of 30 mAs is usually chosen for the product of the tube current and total scanning time; and 90-120 kV for the tube voltage value. These numbers are coherent with low-dose CT measurement parameters, as used in a study of the radiation exposure of patients in PET/CT [80], where low-dose protocols included tube voltages of 110-120 kV and a product of the tube current and total scanning time of 30-60 mAs.

4.2.2. CT Examinations' Data Records

Three Radiology departments were visited, in order to complete this study on the Optimization principle applied to CT procedures. However, the bulk of the study focused on paediatric CT

procedures in two Portuguese pediatric hospitals. For confidentiality reasons, the paediatric hospitals will not be identified in this work and will be named “Hospital H1” and “Hospital H2”.

Two different sets of data were collected, provided by the visited Radiology departments in the two pediatric hospitals. For each set, only the head, chest and abdomen CT examinations were selected for analysis, for both pediatric and adult procedures. The examinations selected for analysis constitute two different sub-sets, which will be studied in this work and referred to, from now on, as Data Set 1 (from “Hospital H1”) and Data Set 2 (from “Hospital H2”). More details on Data Sets 1 and 2 are provided in Figure 4.7 and Figure 4.8:

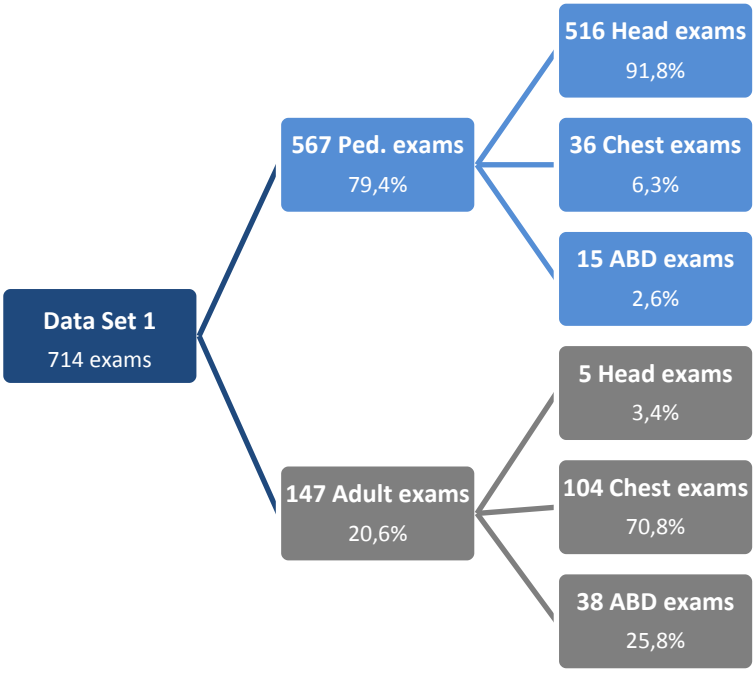


Figure 4.7 – Diagram of the selected pediatric and adult examinations for analysis (Data Set 1).

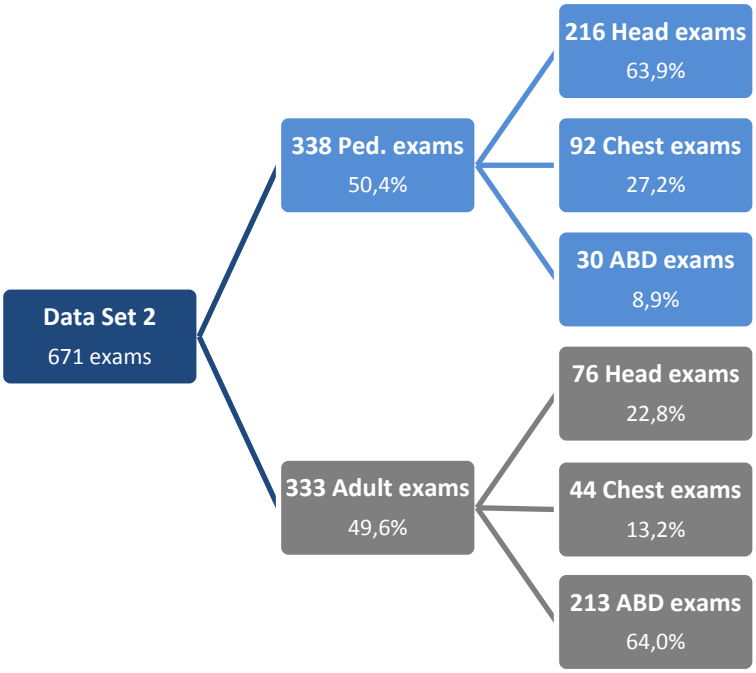


Figure 4.8 - Diagram of the selected pediatric and adult examinations for analysis (Data Set 1).

The following parameters were collected for all CT examinations:

- Type of examination;
- Age (years);
- Gender;
- Tube voltage (kV);
- Tube current (mA) or product of tube current and time (mAs) – depending on the equipment;
- Pitch[7];
- Rotation Time (seconds);
- Slice width or scan length – depending on the equipment (cm);
- $CTDI_w$ or $CTDI_{vol}$ - depending on the equipment (mGy);
- DLP (mGy·cm).

In particular, for Data Set 1, the collected scan length values often appeared to be incorrectly registered in the institution's data records. The author evaluated these data, in order to determine if

[7] Pitch values were not actually included in the hospital's original records, they were determined by the author, based on information related to other used acquisition parameters (table movement and beam width).

they agree with typical values for the irradiated length, considering the anatomical region being scanned. The author established "normal" (expected) values herself, taking into account both Swiss DRLs[8] [81] and the mean scan length values actually used in the institution's equipment (as registered by the CT scanner software):

Table 4.2 – Standard scan lengths used in different CT examinations and age groups, as estimated by the author.

Age Group (years)	Head	Chest	Abdomen
0-1	10-12 cm	12-15 cm	~20 cm
2-5	~13 cm	~20 cm	~30 cm
6-9	~14 cm	~25 cm	~35 cm
10-18 and Adult	15-18 cm	30-40 cm	40-50 cm

While length values lower than to the ones specified in Table 4.2 were considered for analysis (as the scan may comprise only a part of the respective anatomical region), scan length values that exceed the average length value or the upper limits in Table 4.2 were considered invalid for the purposes of this study, for not complying with the standard values. This criterion reduced the number of CT examinations in the seven groups defined for Data Set 1, as shown in Table 4.3. The implications of this reduction on the samples' size will be addressed in the next chapter (Discussion).

Table 4.3 – Number of examinations within each group of Data Set 1, after data validation (considering the scan lengths used).

	Data Set 1 Group	Original Nº of exams	Invalid Data (%)	Remaining Valid Data (%)
PEDIATRIC	Head	516	165 (32,0%)	351 (68,0%)
	Chest	36	4 (11,1%)	32 (88,9%)
	Abdomen	15	0 (0%)	15 (100%)
ADULT	Head	5	1 (20%)	4 (80%)
	Chest	104	3 (2,9%)	101 (97,1%)
	Abdomen	38	4 (10,5%)	34 89,5%)

[8] Actually, the DRL values consulted do not actually express the values of the scan lengths used, but they can be easily determined using the $CTDI_{vol}$ and DLP reference values, as expressed by Equation 3.4).

4.2.2.1. Comparison between Portuguese Examinations and International (Swiss) DRLs

The Dose Reference Values (DRLs) define local reference values, which are set for a standard procedure and groups of standardized patients (or dose phantoms). The DRLs are recognized internationally as a tool to identify situations where the radiation exposure of patients is above the standard practices. A DRL is not be considered as a dose limit or as an optimal dose value, but it should not be exceeded without justification in routine procedures [81].

To establish conformity with the DRLs, the parameter being studied ($CTDI_w$, $CTDI_{vol}$ or DLP) is compared to the numerical value of the DRL. Usually, the 75th percentile (P75) of the distribution is used for this comparison, instead of the mean:

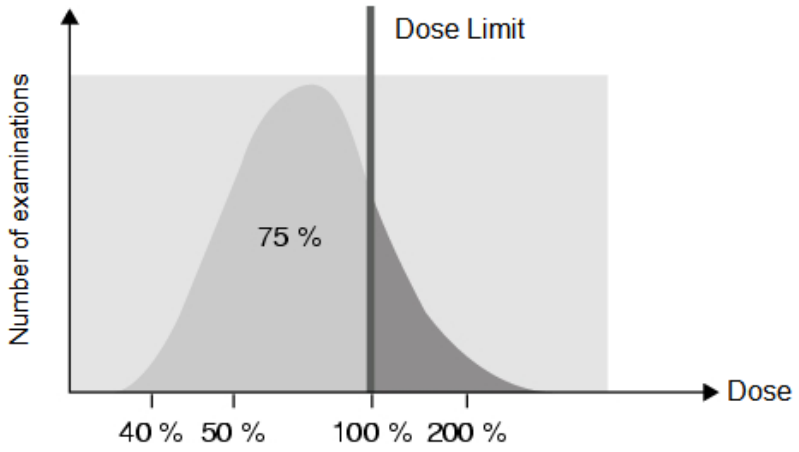


Figure 4.9 – Schematic representation of the 75th percentile, for a given dose distribution.

From the data comprised in data sets 1 and 2, the $CTDI_{vol}$ was determined from the $CTDI_w$ according to Equation 3.3 (see section 3.1.5). The P75 of the distribution of $CTDI_{vol}$ values was then determined for each examination type (head, chest and abdomen procedures) and for different age groups, in both data sets.

Unfortunately, Portuguese DRLs are yet to be established and so the $CTDI_{vol}$ distributions of data sets 1 and 2 were compared with the Swiss DRLs[9]. Table 4.4 lists the 75th percentiles for the head, chest and abdomen examinations comprised in data sets 1 and 2 and the correspondent Swiss DRLs. The age intervals considered in Table 4.4 correspond to the age groups defined for the Swiss DRLs [81]:

Table 4.4 – The calculated $CTDI_{vol}$ (mGy) 75th percentiles of "Hospital H1" and "Hospital H2" and the correspondent Swiss DRLs **[**81**]**, for head, chest and abdomen procedures.

Age Group	HEAD			CHEST			ABDOMEN		
	H1	**H2**	**DRL**	**H1**	**H2**	**DRL**	**H1**	**H2**	**DRL**
[0]	22,43	51,18	33	3,72	0,99	3,5	1,27	-	5
[1-5]	27,1	51,62	40	2,87	4,31	5,5	2,87	4,8	8
[6-10]	38,6	51,78	50	2,73	3,04	8,5	14,69	9,56	13
[11-15]	41,7	61,67	50	4,48	6,47	6,8	6,47	8,28	10
[16+]	41,7	61,8	65	7,2	9,23	10	8,47	12,98	15

The grey-highlighted values on Table 4.4 correspond to the data sets' p75 values that are higher than the correspondent Swiss DRLs. More information on the Swiss DRLs and the $CTDI_{vol}$ distributions considered can be found in Appendix II. The data listed on Table 4.4 are represented next, on the graphics of Figure 4.10, Figure 4.11 and Figure 4.12 (for head, chest and abdomen examinations, respectively):

[9] Although the Swiss values do not represent *local* reference values, they are used for the purposes of this analysis as an *European* reference.

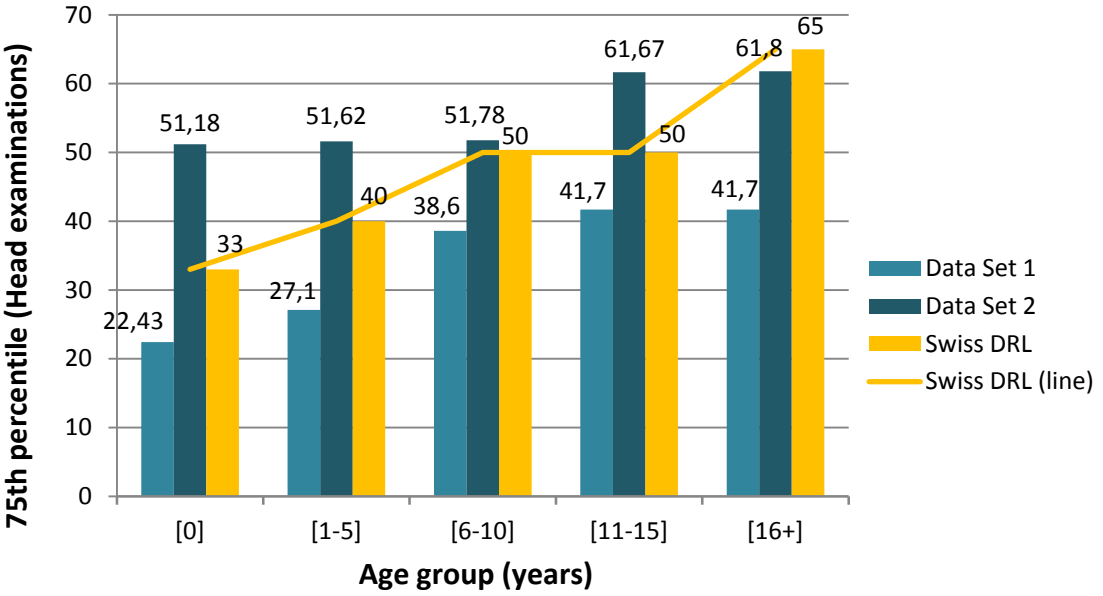


Figure 4.10 – Comparison between the $CTDI_{vol}$ (mGy) 75th percentiles of Data Sets 1 and 2 and the Swiss DRLs [81], for head CT examinations.

In Figure 4.10, the p75 values of Data Set 2's [0], [1-5], [6-10] and [11-15] age groups exceed the correspondent Swiss DRLs. All of the Data Set 1's p75 $CTDI_{vol}$ values are lower than the Swiss DRLs.

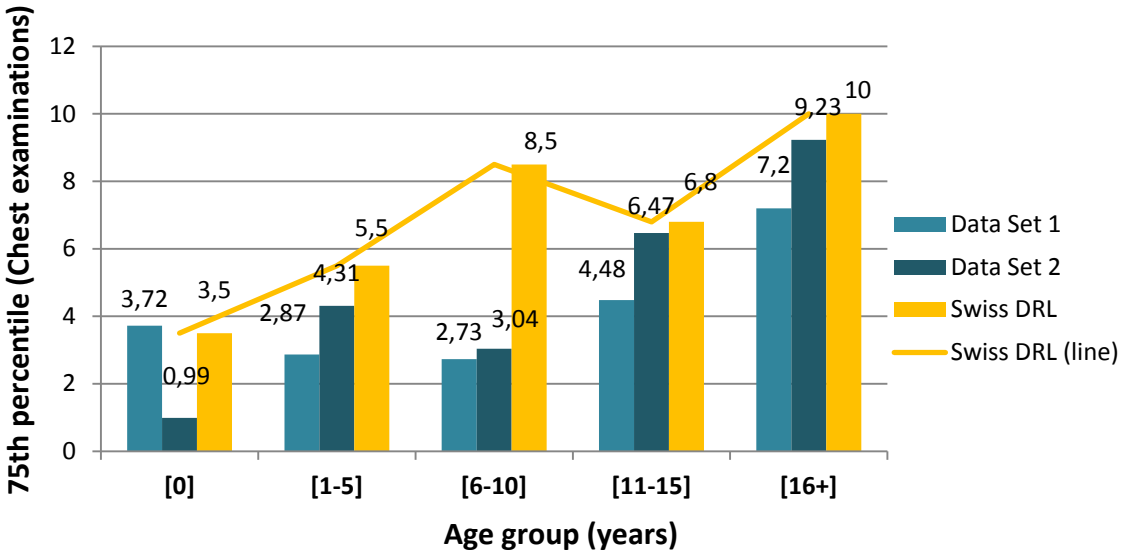


Figure 4.11 – Comparison between the $CTDI_{vol}$ (mGy) 75th percentiles of Data Sets 1 and 2 and the Swiss DRLs [81], for chest CT examinations.

In Figure 4.11, the p75 value of Data Set 1's [0] age group exceeds the correspondent Swiss DRL. However, this p75 value is only slightly higher than the DRL value (3,72 *vs.* 3,5 mGy) and there are

only 2 examinations in this age group distribution (see Appendix II), which the author considers not to be a representative and statistically significant sample size. All the other p75 $CTDI_{vol}$ values of Figure 4.11 are lower than the Swiss DRLs.

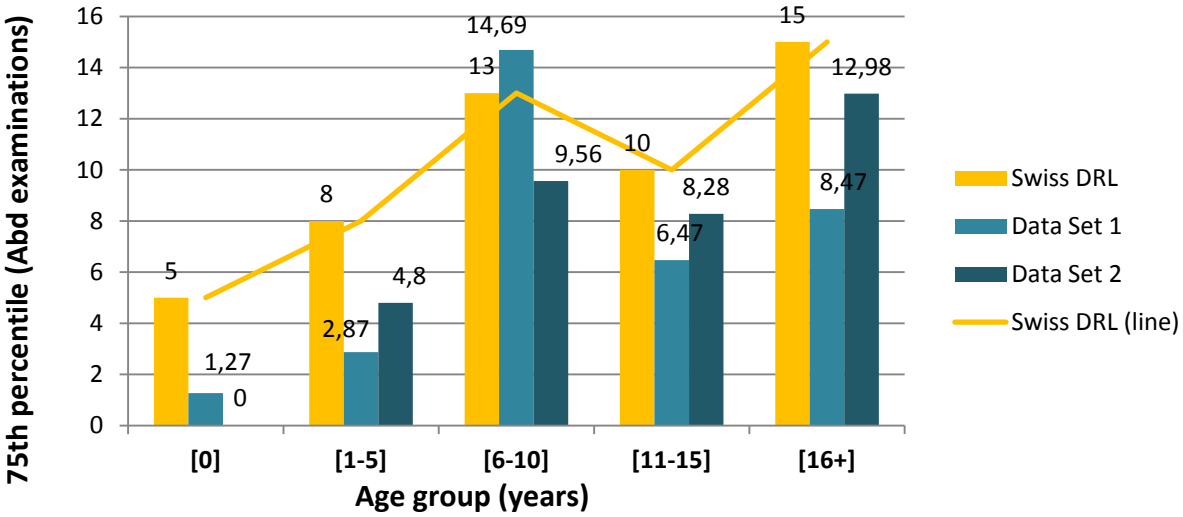


Figure 4.12 – Comparison between the $CTDI_{vol}$ (mGy) 75th percentiles of Data Sets 1 and 2 and the Swiss DRLs [81], for abdomen CT examinations.

In Figure 4.12, the p75 value of Data Set 1's [6-10] age group exceeds the correspondent Swiss DRL. However, this p75 value is only slightly higher than the DRL value (14,69 *vs.* 13 mGy) and there are only 4 examinations in this age group distribution (see Appendix II), which the author considers not to be a representative and statistically significant sample size. All the other p75 $CTDI_{vol}$ values of Figure 4.12 are lower than the Swiss DRLs.

4.2.2.2. Comparison between Portuguese Examinations and International Dose Studies

From the data comprised in data sets 1 and 2, effective doses were estimated according to the following calculations:

- When the $CTDI_w$ was the parameter given, $CTDI_{vol}$ was determined using Equation 3.3 (see section 3.1.5);
- From the $CTDI_{vol}$ value and the scan length, the DLP was determined, using Equation 3.4;
- Finally, effective doses were estimated, multiplying the DLP value by the correspondent conversion factor (see Table 4.5), as expressed in Equation 3.5.

Table 4.5 – The DLP-Effective Dose conversion factors (for adult and pediatric head, chest and abdomen examinations) considered in this work [82].

Age Group (years)	Head conv. Factor	Chest conv. Factor	Abd conv. Factor
0-1	0,011	0,039	0,049
2-5	0,0067	0,026	0,03
6-9	0,004	0,018	0,02
10-18	0,0032	0,0013	0,015
Adults (18+)	0,0021	0,014	0,015

The estimated mean effective doses of both data sets were compared with the values reported in two international studies: a pediatric Belgian multicentre study [83] and an American survey on adult examinations [84] [10]. The objective of this analysis is to assess how the Portuguese patient doses relate to the ones of other countries. Only the effective doses from head examinations will be presented in this analysis:

- The Belgian study mentioned above [83] was executed in 7 medical centers, but only 3 of them (the ones where age-adapted CT protocols are used) are considered for the purposes of this analysis. This Belgian study reports effective doses values for 1-, 5- and 10-year-old children, and so examinations on children of those same ages were selected from data sets 1 and 2. The graphic of Figure 4.13 depicts the estimated mean effective doses of the head examinations comprised in Data Sets 1 and 2 and in the 3 Belgian institutions considered:

[10] Information on the protocols used and the populations studied on both these international studies can be consulted in Appendix III.

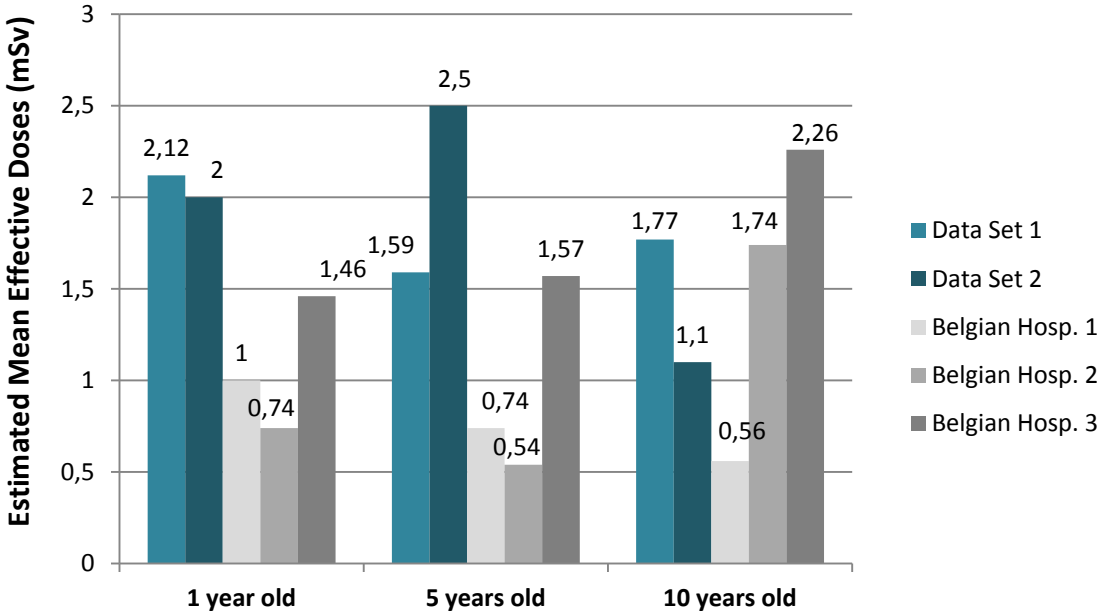


Figure 4.13 – Comparison between the estimated mean effective doses of the pediatric head CT examinations comprised in Data Sets 1 and 2 and the doses reported for 3 Belgian medical institutions [83], for the ages of 1-, 5- and 10-years-old.

In Figure 4.13, the estimated mean effective doses for 1 and 5 year-old children are approximately two times larger in both Portuguese data sets than in the three Belgian institutions. However, the effective dose registered for Belgian Hospital 3 exceeds the Portuguese estimated effective doses in head examinations executed on 10 year-old children, which is probably due to the higher tube current values used for this age group, on that hospital (around 260-300 mA.s) – see Appendix III. On general, all the effective dose values on Figure 4.13 are relatively similar and can be considered appropriate for head examinations (none of the dose values exceeds 2,5 mSv).

- The graphic of Figure 4.14 depicts the estimated mean effective doses of the adult head examinations comprised in Data Sets 1 and 2 and the ones reported in the aforementioned American survey [84]:

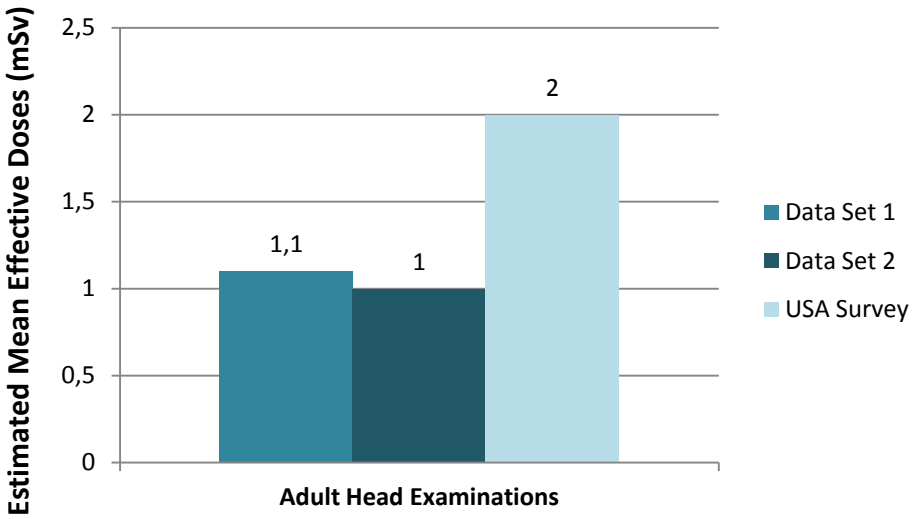


Figure 4.14 – Comparison between the estimated mean effective doses of the adult head CT examinations comprised in Data Sets 1 and 2 and the doses reported in an American survey [84].

For both data sets, the estimated mean effective doses are lower than (around half of) the mean effective dose reported for the American survey considered. According to the information listed on Appendix III, the tube voltage used on the 45 head examinations surveyed by this American study is 127 kV (mean value), which justifies the higher effective dose value (the mean tube voltage value used in both Portuguese hospitals is 120 kV).

4.2.3. Assessment of the CT protocols with phantom measurements

The author had access to the acquisition protocols adopted in the pediatric hospital institution were the CT examinations included in Data Set 1 were performed (the acquisition protocols used for the examinations comprised in Data Set 2 were not available). Hence, phantom dose measurements were carried out on the CT equipment where Data Set 1's examinations were performed. The phantom dose study hereby presented focuses on the most commonly performed CT examinations of that data set: pediatric head examinations, particularly for the younger age groups (newborns and children aged 3 – 24 months).

Table 4.6 lists the institution's standard acquisition parameters used for all age intervals (head examinations):

Table 4.6 – kV and mA values used for head procedures, in the institution where Data Set 1's examinations were executed.

	Age Interval	Tube voltage value (kV)	Tube current value (mA)
Head Examinations	Newborns	120	70
	3-9 months	120	90
	9-24 months	120	110
	2-6 yrs	120	130
	6-8 years	120	150
	>8 and <12 years	120	185
	Adult and > 13 years	120	200

Different phantom dose measurements were executed, varying the tube current and tube voltage values. Firstly, the tube voltage was fixed at 120 kV and acquisitions were made at tube current values of 70, 90 and 110 mA (the standard current values used in pediatric head procedures). Acquisitions were also made at 80 and 140 kV, with the tube current settled at the fixed values of 75 and 77 mA, respectively. The kV-mA combinations used are displayed in Table 4.7. Other technical factors (such as the pitch value, scanned length and slice width) where chosen in a way that tries to replicate a standard acquisition protocol used for pediatric head procedures, as they are usually performed in this CT unit.

Table 4.7 – Head phantom dose measurements: $CTDI_{vol}$ for each kV-mA combination.

Tube voltage value (kV)	Tube current value (mA)	$CTDI_{vol}$ (mGy)
80	75	9,79
120	70	35,63
120	90	44,68
120	110	56,73
140	77	55,92

An integrating electrometer, a standard CT- dosimetry phantom and a pencil-type ionization chamber with an active length of 150 mm were used. The phantom is made of PMMA, with a diameter of 160 mm, contains five holes (one at the center, and the other four just below the

cylinder surface, at 90° intervals) with a diameter of 10 mm, on which the ionization chamber is placed (see Figure 4.15). A term defined as the dose profile integral (DPI) is given at the output of the electrometer. This value represents the radiation dose profile as it is detected by the probe, along the CT rotation axis, which is integrated in order to determine the $CTDI_{100}$ (see Equation 3.1).

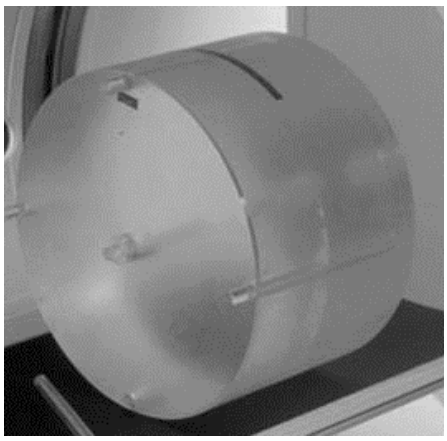
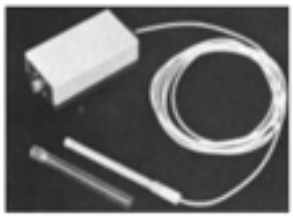
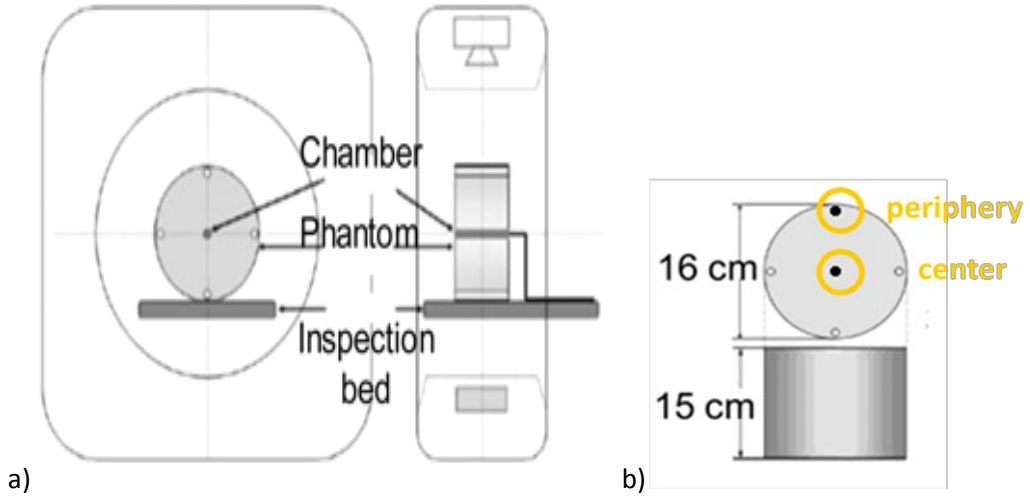
a)  b) 

Figure 4.15 - a) 160 mm PMMA head phantom, adapted from [85] and b) pencil-shaped ionization chamber, adapted from [86].

With the holes of the phantom located parallel to the rotation axis, the ionization chamber was positioned both at the center of the phantom and at its periphery (on the upper hole), as depicted on Figure 4.16. Both these measurements are necessary to derive the $CTDI_w$ from the $CTDI_{100,}$ as defined by Equation 3.2. Finally, the $CTDI_{vol}$ was determined from the $CTDI_w$ value, as described by Equation 3.3.



a) b)

Figure 4.16 - a) Position of the phantom within the gantry and b) position of the ionization chamber within the phantom. Adapted from [86].

The procedure explained below follows the instructions of an American document [87], which provides guidance in either the development of CT protocols for children, or the verification that the currently used protocols are adequate:

1. First, the $CTDI_{vol}$ for a FDA's 16 cm PMMA head phantom is determined and compared with the ACR's adult reference value of 75 mGy [88]. In the case of the present study, only pediatric $CTDI_{vol}$ values were estimated, for different tube voltage and tube current values, as listed on Table 4.7. In particular, the kV-mA combinations with 70, 90 and 110 mA correspond to the institution's standard parameters used for the age groups comprising of newborns, children aged 3-9 months and children aged 9-24 months respectively, as can be consulted in Table 4.6.

2. Next, baseline techniques for an adult head examination are established and recorded. The appropriate mAs (the product of tube current and rotation time) values for pediatric head procedures (in particular, newborns and children aged 1 and 5 years) are then determined by multiplying the adult baseline value by a reduction factor. The determined reduction factors are listed in Table 4.8, on which the grey-highlighted lines indicate the baseline parameters, used in a standard adult head examination, for the institution being studied – in this case, 120 kV and 200 mA:

Table 4.8 – The mA·s' reduction factors for pediatric head examinations. Adapted from [87].

Head Baseline	**kV** = 120	**mA** = 200	**Time** = 1 sec	**Pitch** = 1
Thickness[11] (cm)	**Approx. Age**	**mA·s reduction factor**	**Estimated mA·s = baseline x red. Factor**	
10-12	Newborn	0,74	148	
12-13	1 year	0,86	172	
13-15	5 years	0,93	186	
15-18	Standard adult	**Baseline:**	200	

[11] The original thickness values in [85] are substituted in this table by the expected scan lengths for the CT equipment being concerned, as was previously addressed in Table 4.2.

5. Discussion

5.1. Nuclear Medicine and PET/CT Dose Optimization

5.1.1. Visited Nuclear Medicine Facilities general features

Existence of Internment Units

As mentioned in the previous chapter, only one of the visited Nuclear Medicine departments encompasses an internment unit, for patients to whom are administered high activities and cannot be immediately discharged. It is important to mention the Portuguese legislation on this matter [79] for ambulatory patients, the measured dose rate at one meter from "hot" zones (in this case, the surface of the patient) cannot exceed the established dose limits for the general population and, in the case of ^{131}I therapy, the maximum activity allowed is 740 MBq (20 mCi) - otherwise, patient internment is required.

Exposure of Pediatric Patients

In order to reduce the exposure of pediatric patients, all the visited institutions book one day, or a fraction of a day, for pediatric exams only. This is particularly important from a Radiation Protection point of view, since this methodology protects children from injected adult patients, whose activities can be very high and harmful for an infant in the proximity. Furthermore, a "pediatric day" turns out to be more comfortable for the children themselves, and older patients as well; it is also simpler for the technologists, given that the approach to the patient is considerably different, and often pediatric examinations take a longer time to be completed. The percentage of pediatric patients is relatively low amongst Nuclear Medicine institutions because, unlike radiological procedures, nuclear diagnostic examinations are a somewhat rare indication in children's pathologies - apart from Nephrology examinations, which are regularly prescribed in Pediatrics.

Layout of the Services – Area Classification, Location and Occupancy

Most of the visited departments have their different functional areas organized by increasing level of activity as indicated in the respective Portuguese legislation [79], in a way that controlled areas are located as far as possible from the entrance of the department (see Figure

4.3). This structural organization (as well as the controlled access to certain areas, such as the "hot lab", where radiopharmaceuticals are prepared) is extremely important for the Radiation Protection of patients and members of the public, as it makes it difficult for someone to walk around the Nuclear Medicine department and accidently enter a high-radiation area. Additionally, the uptake and imaging rooms should be located as far as possible from - and never adjacent to - uncontrolled areas with high occupancy levels (like waiting rooms for non-injected patients and other members of the public). These Radiation Protection principles are observed in the more recent institutions, but of course that older departments were not built according to this “ideal” organization of a Nuclear Medicine department.

Monitoring of Radiation Levels

The majority of the visited institutions have radiation detection equipment to monitor the radiation levels and instantaneous ambient dose rates in active (or "hot") areas; most of them additionally monitor area radiation levels and dose rates in passage aisles (which are generally classified as “cold”, non-active areas) – depending on the organizational structure of each Nuclear Medicine unit.

Radioactive Waste Management – Separate Sewage System

Special sanitary installations for injected patients are mandatory only where radiopharmaceutical therapy with patient internment is executed, but some of the visited institutions (performing exclusively diagnostic examinations and ambulatory treatment of patients) encompass this special toilet room as well.

5.1.2. Patient Dose Optimization

Waiting Rooms for Injected Patients

One of the most important aspects to take into account in Nuclear Medicine is the fact that the injected patient becomes a mobile (and free-willed) source of radiation. Hence, the Radiation Protection and Dose Optimization of the patient, and others around him, depend on the recommendations and instructions provided to him/her. Injected patients are recommended to urinate frequently and to remain well hydrated either before or after the scanning procedure, because this accelerates the biological elimination of the administered radiopharmaceutical (most of the radiopharmaceuticals used in Nuclear Medicine - and ^{18}F-

FDG is one example - are eliminated through the renal system). Conventional Nuclear Medicine patients are also told to leave the institution, and then return for the scanning process, in order to reduce the irradiation of other patients, professionals and members-of-the-public within the Nuclear Medicine department. As an alternative, Nuclear Medicine departments generally include an exclusive waiting room for injected patients, in order to separate them from the general population and workers. The irradiation of other people, by proximity to an injected patient, is not that much of an issue in PET examinations, since patients remain in a rest chair, within a controlled area inside the institution, to reduce ^{18}F-FDG uptake in skeletal muscles.

Patient Management

It was mentioned in the previous chapter that often patients are grouped by age, or type of examination. Because several radiopharmaceuticals (such as ^{18}F-FDG) are supplied by an external provided, once or twice per day, the scheduling of patients ought to be very well organized. The scanner occupancy and the radiopharmaceutical doses are optimized by keeping a continuous flow of patients: while one patient is in the scanner, the next one is waiting, in the uptake phase. One other way to optimize the activity that one ^{18}F-FDG supply yields is to accordingly adapt the patient order - heavier patients go first, in order to "spare" the remaining activity existing in the FDG supply.

The majority of the institutions does not feature specific areas for pediatric patients (as this is only mandatory, according to the Portuguese legislation [79], in institutions where radiopharmaceutical treatment with patient internment is performed) and so frequently children and injected adults have access to the same rooms. The scheduling of a "pediatric day", as stated before, represents one way to overcome pediatric exposure (caused by proximity to an injected adult patient).

Radiopharmaceutical Administration

As in other international Nuclear Medicine centers, radiopharmaceutical administration is mostly based on patient weight and the EANM's established maximum limits. Amongst the administered drugs, diuretics are of particular relevance for the Radiation Protection of the patient, since most of the radiopharmaceuticals used in Nuclear Medicine are eliminated through the kidneys. Immediately before the scanning process, the patient is instructed to

void, in order to clear the radioactivity that has accumulated in the bladder (which is approximately 15% of the administered activity [89].

Patient Dosimetry

In summary, the visits to the Nuclear Medicine departments allowed the identification of a few operational aspects that should be better implemented for Dose Optimization and Radiation Protection purposes:

- An adequate separation (different areas) for injected patients and non-injected patients, including a specific area for pediatric patients only
- The recording of the estimated patient dose, for each examination
- The implementation of a national recording system of patient examinations, administered activities and associated estimated doses.

5.1.3. Workers´ Dose Optimization

Individual Monitoring of Workers

When it comes to the individual monitoring of workers, professionals who directly handle radiopharmaceuticals are controlled for extremities' dose, using a ring dosimeter (and sometimes, an additional wrist dosimeter as well). These individuals are normally classified as category A workers, in the terms of the national and international legislation [90], and so they have to be monitored monthly, either for extremities and whole-body doses. Category B professionals, who have access to controlled and supervised areas but yet are not liable to receive radiation doses (in excess of 6 mSv/year) that would have them classified as category A workers, are monitored as well, but only for whole-body dose and with a quarterly periodicity. This monitoring of category B professionals is necessary, at least for the purpose of demonstrating that the worker is correctly classified in this category [91].

As reported by the contacted professionals, dose limits for the exposed workers are hardly ever exceeded. Most of the institutions determine intermediate dose limits (monthly limits, for instance) to be followed in the institution, as a guide for keeping track of the cumulated annual doses.

Unfortunately, exposed workers usually ignore the total amount of activity handled and administered and the indicative doses they are daily exposed to.

From the dosimetric records provided by one of the visited institutions, one can infer that the average equivalent dose (Hp (10)) and skin dose (Hp (0,07)) of category A workers, both of 0,24 mSv, are well below the established dose limits (500 mSv/year is the limit for skin dose; and 20 mSv/year the average limit for the effective dose). In addition, the null values observed for category B workers were expected, as these workers (who generally perform administrative work, image processing or similar "desk" functions) rarely stand in the proximity of radiation sources. The mean Hp (10) value of 1,08 mSv, for 21 category A workers, is also fairly distant from the 20 mSv limit. The author believes that the implemented Radiation Protection practices, particularly the rotation of personnel and the application of the three basic aspects of Radiation Protection (time, distance and shielding) contribute to these low radiation doses, which don't even reach one tenth of the established dose limits for exposed workers. In addition, as expected, those technologists involved in medical tasks requiring the proximity to an injected patient, such as the radiopharmaceutical administration, and patient accompaniment, are the ones most exposed and with higher values of annual dose.

Optimization of the Exposure Resulting from the Administration of Radiopharmaceuticals

One of critical aspects to achieve dose optimization and reduction of the exposure of professionals is related to those workers who administer the radiopharmaceutical to the patients.

- <u>Use of syringe protections</u>

  Syringe protections are not always used, because they complicate the injection process, particular in chemotherapy patients, whose veins are often collapsed, or babies and very small children, whose veins are hard to detect.

- <u>Education and training of staff</u>

  Also, this administration is often performed by different staff professional groups -Nuclear Medicine technologists, nurses and in some cases (such as melanomas), medical doctors physicians). This should be a matter of concern because these different classes of professionals have different levels of education and training in Radiation Protection

related issues. If possible, the radiopharmaceutical administration should be restricted to Nuclear Medicine technologists, even if they need additional training, for special injections. Either way, the professional classes who are attributed the radiopharmaceutical injection should be the same in all institutions.

- Organizational aspects, experience

  A rotation system between workers is always implemented in Nuclear Medicine departments, in order to reduce the radiation dose each individual is exposed to. Nevertheless, in some of the visited institutions, a few "difficult" tasks – such as the radiopharmaceutical injection to small children and chemotherapy patients – are normally assigned to experienced professionals. Although this may represent an additional exposure of those workers, they do administrate the radiopharmaceutical faster than younger, inexperienced workers do, and so the amount of *time* (one of the three basic aspects of Radiation Protection, as mentioned in section 2.3.1) of exposure of workers is minimized.

Optimization of the Exposure Resulting from the Manipulation and Preparation of Radiopharmaceuticals

- Use of syringe protections and shielding

  Syringe lead or tungsten shields, which dramatically reduce the doses to the extremities are not always used by workers as they render the weight of the syringe much higher and complicate their manipulation;

- Use of tongs

  As *distance* is another basic aspect of Radiation Protection, tongs are frequently (but not always) used to increase the distance to radioactive sources, such as vials or syringes and to reduce the dose to the extremities of the workers;

- Use of portable shielding systems, glove boxes and other protective systems

  The third Radiation Protection aspect to consider is *shielding*: shielding glasses and glove boxes are always used during the radiopharmaceuticals preparation and storage and in the

shielding of patients in PET uptake rooms. Additionally, portable lead shields are usually used to move radioactive sources within the department.

Adequate Structural Shielding Design

Obviously, structural shielding and protective barriers must be adequate for the radionuclides and energies to be used: the highly penetrating energies used in PET (^{18}F) require a significantly barrier thickness, for the attenuation of 511 keV gamma photons, when compared to the required thickness of shielding for other conventional Nuclear Medicine radionuclides, such as ^{99m}Tc (140 keV gamma rays).

The Risk of Contamination

Whenever there is a risk of contamination in benches and radiopharmaceutical handling areas, the radiation doses, and well as their distributions in the body ought to be assessed [91], and for this purpose workplace dose measurements can be coordinated with individual dose measurements, in order to estimate individual doses. Although this type of incidents is usually registered in the institutions' records, routine contamination monitoring and control is not implemented as a "good practice" – being only performed following an incident or when there is a suspect that a contamination has occurred.

Students and Apprentices

The dose limits for apprentices and students aged 18 years or over are the same as the dose limits for exposed workers [90,91]. For this reason, if a student has access to the controlled and supervised areas within a Nuclear Medicine institution for extended periods of time, his/her radiation dose is recommended to be monitored just as the doses of radiation workers (whole-body and extremities dosimetry, when appropriate). The dosimetric service responsible for these students' monitoring can either be the service used by the Nuclear Medicine facility, or one set by the student's institution. As an example, for the purposes of this work, the author had access to controlled areas within several institutions, and dose monitoring was implemented according to the preferences of each department – both direct-reading dosimeters, belonging to the department, and an individual dosimeter specially attributed to the student by her institution, were used. Of course that the radiation doses the author received were extremely low – the total of time spent within controlled areas, considering all the visited Nuclear Medicine institutions, was inferior to two weeks – but, in the case of

Nuclear Medicine appendices who spend several months in those areas, this monitoring process is fairly more uniform: they are attributed a single individual dosimeter, and use it at all times.

Summary

In summary, in order to successfully implement Optimization principle leading to a reduction of dose to the workers, some good practices must be operational, such as:

- Use of syringe shielding during preparation and administration;
- Use on tongs during manipulation
- Shielding of staff by means of protective barriers and accessories, including mobile shields;
- Monitoring of dose to the extremities, using ring or wrist dosimeters;
- Knowledge and routine recording of the manipulated activity;
- Manipulation and administration of radiopharmaceuticals must be performed by adequately trained professionals; ideally only qualified Nuclear Medicine technologists should handle radioactive sources;
- An adequate register and monitoring of the workplace dose rateThe existence of a Radiation Protection Committee in the facility (already implemented in some of the visited institutions);
- Regular monitoring of staff for internal contamination, after handling radioactive volatile materials (although an exhaustive practice, it is certainly safer);
- Individual monitoring and dosimetry of students and apprendices.
- It must be stressed that not all of these practices were correctly implemented or operational or systematically used in all the Nuclear Medicine services visited.

5.1.4. Dose Optimization for the Members-of-the-Public

Discharge of the Patient

Before the injected patient is discharged from the Nuclear Medicine institution, instructions on how to maintain doses to other individuals (family members and other members-of-the-public) as low as reasonably achievable – as states the ALARA principle – are usually given to

him, sometimes in a written form (depending on the administered activity) [92]. For therapeutic purposes, written institutions are mandatory by national legislation [79], whilst in diagnostic procedures a simply explanation is considered sufficient, for the patient to understand the risks of exposure that the people in his/her proximity are subject to.

Some of the Nuclear Medicine professionals reported that a common practice, in the release of diagnostic patients, is to explain to the patient only what is strictly necessary: pregnant women and children ought to be protected, reducing to the strictly necessary the time spent close to the patients; however, other Radiation Protection recommendations, such as avoiding close contact with members-of-the-public in public transportations or crowded places, are sometimes omitted". Nevertheless, despite activity values that permit the patient to be released from the institution (in ambulatory and diagnostic procedures), the facility is still responsible for ensuring that the exposure of members-of-the-public is as low as reasonably achievable, and hence the importance of the instructions given to the patient.

While injected patients are always discharged immediately after the examination is completed in diagnostic and ambulatory procedures, radiopharmaceutical therapy involving higher activities may require the admission of the patient in the institution, for one or two days. Usually, the value of 740 MBq is the decision criterion, to decide whether the treated patient should remain at the hospital, or if he/she can be released as an ambulatory patient.

Separate Waiting Room for Injected Patients

Generally, the radiation doses of members-of-the-public within a Nuclear Medicine institution, from the proximity to injected patients who undergo a single examination, are too low for any type of monitoring or individual protection to be considered. In particular, family members who accompany a patient (children, in particular) during the examination are usually in close contact with that patient for a great part of the day, and so it wouldn't be of great interest to control the radiation dose of that person only while he/she remains in the hospital. The proximity to injected patients is only problematic when it happens every day – thus, for workers. However, this is still an important Radiation Protection topic to discuss: the radiation doses received by members-of-the-public standing near injected patients ought to be at least estimated, because, after all, it is a considerable portion of the population that could be eventually exposed, considering all the examinations performed each day, at present.

Injected patients waiting for the examination, if they cannot leave the institution for a while, should be isolated from members of the public and other patients, in an exclusive waiting room which, according to the Portuguese legislation, must allow for 2 m^2 per patient [79]. This room exists in the majority of the visited hospitals, but it is always preferable for the patient to leave the institution after he/she has been administered the radiopharmaceutical (in conventional Nuclear Medicine examinations), so he/she does not represent an additional radiation source within an already high-radiation area. This practice is helpful when it comes to the protection of other patients, members-of-the-public and specially workers, who remain within the institution all day. In PET examinations, the whole "route" of the patient, within the institution, from the moment he/she enters the facility to the discharging, is fairly well controlled – mainly because he/she must remain at rest, in an uptake room, while waiting for the examination.

Finally, the Radiation Protection issues involving members-of-the-public which implementation requires, in the perspective of the author, some harmonizationand optimization in the NM services visited are:

- The existence of specific areas for members-of-the-public, separated and far from the injected patients' areas, if possible;
- The reduction of the time that carers and family members spend in close proximity to the patient, within the facility;
- The reduction of the time that family members spend near the patient, at home – depends on the instructions given to the patient.

5.2. CT Dose Assessment and Optimization

Unlike the previous study on (dose) optimization in conventional Nuclear Medicine and PEC/CT examinations where internal dosimetry methods and biokinetic models are used to assess the organ doses following the incorporation of a radiopharmaceutical substance, in CT examinations, the patient is exposed to an external radiation source during a controlled and well defined time interval and it is possible to perform a more accurate assessment of the effective dose the patient is exposed to. Furthermore, the patient is, in most of cases, only

partly irradiated, as only a single anatomical region (head, thorax, abdomen, etc.) is being scanned. As generally physical barriers protect professionals, the great concern is about patient exposure. It should be stressed that the exposure of the members-of-the-public, in the framework of CT examinations, is associated mainly to the examinations performed to pediatric patients, when a family member often needs to remain close to the child, during the image acquisition process.

5.2.1. Data Recording Methodologies vs Data Quality

The groups selected for analysis (Data Sets 1 and 2) were created from two data sets collected from the visited hospital's databases, which encompass head, neck, ears, abdomen, pelvis and extremities procedures, amongst other examination types. Data Sets 1 and 2, however, include only the performed head, chest and abdomen examinations as these are the most commonly performed and studied CT procedures worldwide.

In pediatric CT, the brain is the most frequently imaged anatomical region, especially in younger group ages (children of 0 to 24 months) while, in adult CT, abdomen and chest are the most common procedures. This is because an exposure of newborns and very small children is necessary (and justifiable) when there is a suspicion of a congenital neurological malformation, which would be detected in the first two years after the child is born. Older children and teenagers, on the contrary, are mostly prescribed other types of examinations (extremities and thorax, probably due to injuries and bone fractures). Chest and abdomen CT-procedures are frequent, and sometimes repeated, in adult patients because they are often indicated for the diagnosis of pathologies, such as cancer, that appear later in life.

While, in Data Set 1, examination data was registered on paper, by the Radiology technologist who executes the CT examination, in Data Set 2 this information is recorded in a digital database. These distinct registry methodologies shed light on the need to the standardize and automatize the recording of the information about the performed examinations. Indeed, amongst the hand-written records from which Data Set 1 was constructed, non-infrequently the information such as the examination type or patient age was lacking. *A posteriori*, more exhaustive analysis data sets led to the rejection of a considerable amount of examinations data – around 30% of the original number of head, chest and abdomen examinations, listed on

Figure 4.7. These 30% were eliminated because they did not contain the necessary information for the estimation of effective doses (namely, the scan length, pitch and $CTDI_w$ values used).

For Data Set 1, highly improbable scan length values were registered, considering the type of examinations being studied. These data were either incorrect or mis-registered, and modified by the author according to established normal intervals for scan lengths, in conformity with both international reference levels (Swiss DRLs) and the real scan length values registered in the equipment. As explained before, scan length values below these theoretical intervals were not invalidated, because the scanning of only a portion of the body region – in this case, head, chest or abdomen – is rather common. Any length value that exceeded these intervals was considered by the author to be an unacceptable, abnormal number, and therefore invalid for the purpose of effective dose assessment. In reality, some of these values could actually be considered for analysis, given that they do not deviate much (5-10% above the upper limit) from the expected values' interval. These values do exist in CT examinations: in some cases, the irradiated length is indeed superior to the standard expected values; however, it really depends on the pathology to be assessed. As these particular cases do not frequently occur, and given that the diagnostic objective of the performed CT procedures is not known by the author (for confidentiality reasons), the author chose to consider only *standard* scan length values in order to assess effective doses in general head, chest and abdomen CT examinations.

The main drawback associated to a manual instead of an automatic, digital registry system, coordinated with the equipment's database, is that sometimes professionals do not write down all the relevant examination parameters used, or write them incorrectly. A digital recording of this information would greatly eliminate human error, and this would benefit future studies to be made on these data – in fact, for the purposes of this study, the most difficult and time-consuming task while analyzing Data Set 1 values was the selection of incorrectly registered data.

5.2.2. Comparison between Portuguese Examinations and International Data

In Figure 4.10, the calculated p75 values for the head procedures of Data Set 2 show that there is a certain similarity between the $CTDI_{vol}$ values of all age groups (around 50-60 mGy), which suggests that similar protocols are being used. A further, more comprehensive analysis of this

data set (which is beyond the scope of this study) would be necessary to understand why these high $CTDI_{vol}$ values occur. For instance, it would be important to know the reason why those head examinations were indicated, the pathologies being studied and the protocols used (no information on Hospital H2' protocols was available), before any conclusion can be draw from these seemingly excessive $CTDI_{vol}$ values.

The majority of all the other p75 values in Figure 4.10, Figure 4.11 and Figure 4.12 are lower than the correspondent Swiss DRLs. Nevertheless, as the Swiss DRLs considered in this analysis are merely an European reference, they represent a rough approximation to what would be the ideal Portuguese reference values. Portuguese and local DRLs are yet to be determined, and only those can effectively be compared with the patient examinations performed in Portugal, so as to assess whether the resulting patient doses are or not superior than the recommended values.

In general, the estimated effective doses of both Portuguese data sets are similar to the ones registered in the Belgian study (pediatric examinations) and in the American survey (adult examinations) considered. None of the Portuguese estimated effective dose values strays afar from the "normal" dose values registered for standard head CT procedures, either on the two international studies considered in this comparison and in the literature (see Table 3.1).

For both Data Sets, the estimated effective doses of pediatric head examinations are higher than the ones estimated for adult examinations, which the author assumes to be due to the small anatomical structures being examined in these procedures – CT technical factors such as the kV or the mA·s product probably need (and are justified) to be higher in this cases, in order to optimize the final reconstruction images' quality.

It is important to note that all the comparisons made between Portuguese and international data are merely a "semi-quantitative" analysis, as all the CT procedures were not executed in the same conditions – the equipments, protocols and technical settings used on the Belgian study and the American survey, as well as the reference population used to establish the Swiss DRLs, are only partly known.

5.2.3. Analysis of pediatric CT protocols

The procedure explained in the previous chapter for establishing new children protocols and/or revising current protocols, originally described in [87], is addressed in this study merely as a possible plan of action for developing future CT dose optimization protocols, to be implemented the Portuguese institutions. It is important to mention that major changes were taking place in the visited Radiology institutions, at the time this work was being developed: all three hospitals are equipped , or will be in a near future, with new, state-of-the-art CT scanners and are therefore still adjusting their Dose Optimization protocols to those recent equipments. For this reason, this work, which focuses on CT-examinations performed using older equipments, does not aim at determining "best acquisition parameters" for the Portuguese institutions being concerned, but only to lay down recommendations to be implemented in the future.

According to the document mentioned above [87], the first step is to verify whether the technical factors used in adult examinations do not deliver estimated radiation doses larger than those recommended by the ACR's CT Accreditation Program [88]. If the measured $CTDI_{vol}$ values from adult head phantom measurements exceed the recommended values of 75 mGy, a reduction of either the tube current or the rotation time might be in order. In hospital H1, phantom measurements using the institution's standard adult acquisition parameters (120 kV and 200 mA) were not executed. At the time that those measurements were performed, the main concern was to adjust the phantom measurements to the pediatric protocols in use and, unfortunately, the measurements could not be repeated later. Therefore, it cannot be confirmed whether the first criteria of this procedure is verified (namely, if the adult standard acquisition parameters result in a $CTDI_{vol}$ value inferior than the one recommended by the ACR). To replace this important step, the $CTDI_{vol}$ values of the four adult head examinations comprised in Data Set 1 can be compared with the ACR's reference $CTDI_{vol}$ of 75 mGy. Three of those four examinations were executed at 120 kV and 200 mA (precisely the acquisition parameters defined for the standard protocols for adult head examinations) and resulted in a $CTDI_{vol}$ of 41,70 mGy. This value suggests that the ACR's reference value is not exceeded for standard adult head examinations and so, in principle, a reduction on the tube current value and/or on the rotation time will not be necessary.

In the next step of this optimization procedure, the acquisition parameters defined for a standard adult head protocol (in this case, 120 kV, 200 mA, 1 second and pitch of 1) are used as a baseline for the establishment of the mAs values to be used in pediatric procedures, as determined in Table 4.8. The estimated values of 148 and 176 mAs for newborn and 1-year aged children, respectively, represent acquisition values that would result in a radiation dose that is approximately equal to or less than the correspondent adult dose for the same examination, provided that all the other technical factors (other than tube current and/or rotation time) remain fixed.

Given that the pediatric protocols used on the CT equipment being studied utilize 70, 90 and 110 mA (with a rotation time of 1 second), it can be concluded that the pediatric doses are currently lower than the correspondent adult doses, when the defined standard acquisition protocols are used. Hence, the pediatric protocols in use are considered by the author to be adequate.

If a reduction on the tube voltage value is chosen instead, for pediatric examinations, the reference mA·s values in Table 4.8 do not apply. Technical guidance for the development of pediatric protocols, concerning the reduction of the tube voltage value is yet to be published. Phantom measurements with fluctuations on the kV value were also executed: the values of 80, 120 e 140 kV were selected, but not much can be inferred from this variation because the tube current value couldn't be fixed at the exact same number (the CT scanner's software automatically adjusts the mA value when the kV value of a standard protocol is altered). Of course that the resulting effective dose is higher when the kV value is increased (see Table 4.7), but there are no reference values and so it is not possible to evaluate whether any reduction on the tube voltage value would produce diagnostically valuable images.

In the analyzed data, a single value of 120 kV was used in practically all the CT examinations, regardless of the anatomical region being studied and the patient's age. Without any consideration on the tube current values being used, a 120 kV value is considered to be problematic by some authors and it has been reported [93], that 120 kV is an excessive value in some children procedures. Nevertheless, the CT equipments of the visited institutions are either very recent or will soon be replaced, and so new acquisition protocols are now being developed and hopefully the tube voltage values will be better suited to patient's age, in the

future. Specially, for Data Set 2, about 15% of the pediatric examinations were executed at a tube voltage value lower than 120 kV (80 or 100 kV), which clearly shows that there is some concern and awareness about the need to reduce the pediatric patient dose, whenever possible.

The ultimate validation of new optimization protocols requires the actual implementation of the suggestions to be adapted in the standard acquisition protocols used in real CT examinations. After the implementation is performed, evaluation of the resulting images' quality by a qualified medical doctor, who would determine if the suggested reductions in the kV and mA·s values produce images with sufficient diagnostic quality.

In conclusion, as was observed in the visited Radiology departments, it is clear that patient Dose Optimization could be implemented and achieved by:

- Recording all the parameters used in CT examinations. The use of a digital and automatic recording system should be mandatory;
- Including the estimation of patient dose in this recording system (the author believes that a regular assessment of patient dose may contribute to the awareness of professionals, concerning the magnitude of patient exposure);
- Using protocols tailored to the patient's age;
- Regular determination of Portuguese DRLs. Such reference levels allow for a straightforward comparison of the dosimetric parameters in CT- examinations and trigger, if these reference levels are exceeded, corrective actions to lower the dose in these examinations;
- Mandatory use of equipment features and capabilities such as Automatic Exposure Control (among others);
- Regular participation of staff in education and training activities, with the purpose of raising their awareness on radiological protection issues.

Finally, concerning the Radiation Protection of workers and members-of-the-public (family members) who accompany CT patients (mostly children) during their examinations, a limitation of the time spent inside the CT scanner room, while the patient is being irradiated, might be considered. The accompaniment of patients must be limited to the situations when it is strictly necessary and adequate shielding, such as protective lead aprons, should be used.

6. Conclusions

The main purpose of this work was to study the Dose Optimization methodologies and strategies implemented in clinical practice, in different Nuclear Medicine and Radiology services in several Portuguese medical institutions. The following objectives were accomplished:

- The radiation exposures and doses to workers in Nuclear Medicine and PET/CT procedures were assessed;
- Patient doses in CT examinations were estimated (particularly in head CT scans) and compared to doses reported in international studies;
- The implementation and operational aspects of Dose Optimization and Radiation Protection principles concerning the patient, workers and members of the public were studied, in the visited medical institutions;
- Clinical practices requiring improvement from the Radiation Protection and Dose Optimization perspectives were identified.

In particular, a few recommendations on optimization were formulated, hopefully of straightforward implementation in clinical practice. Where the patient is concerned, these recommendations include:

- The implementation of a national registry and recording system of patient examinations, containing information about the administered activities, the dosimetric parameters and dose related information and the technical parameters of such examinations. Although different Portuguese stakeholders have already suggested this several times, it was never implemented. Such a system would permit the assessment of the cumulative patient dose and would facilitate the undertaking of dose assessment studies at the national level which are of cornerstone important for the sake of optimization;
- An appropriate and complete recording of all the examinations' parameters used, within each institution. This registry system should be mandatory, digital and automatic and eventually, it would allow for a systematic estimation of patient dose;

- The regular participation of medical staff (medical doctors and radiographers, medical physicists) in education and training activities, with the purpose of raising their awareness about the patient dose topics and issues, as well as to keep abreast of the dosimetric aspects of the clinical practices and equipments used (such as in CT examinations) .

As for the Radiation Protection of workers, the following processes were identified, which require a more thorough implementation of dose optimization:

- The systematic use of syringe shielding during administration, Nuclear Medicine and PET/CT procedures;
- The manipulation and administration of radiopharmaceuticals should be performed exclusively by qualified Nuclear Medicine technologists;
- Staff should be regularly monitored for contamination, each time radioactive materials are handled;
- The regular participation of personnel in education and training activities, with the purpose of raising their awareness to the importance of their own individual dosimetry (the author noticed that usually professionals ignore the cumulative dose to the extremities and the manipulated activities they are exposed to, as result of handling radioactive sources daily).

Finally, concerning the Radiation Protection of members-of-the-public (family members) who accompany patients (mostly children and elderly patients) during their examinations, a limitation of the time spent within controlled areas might be in order. The accompaniment of patients must be limited to the situations when it is strictly necessary and adequate shielding, such as protective lead aprons, should be used.

The author believes that the implementation of the aforementioned suggestions might lead to an improvement in the existing Radiation Protection routines and transform controlled areas within medical institutions into safer radiological environments for patients, professionals and the overall population.

One important inference that can be extracted from the results of this work is that the received dose by a patient who undergoes a single CT, Nuclear Medicine or hybrid (such as PET/CT) examination are far greater than the established yearly dose limit for the public (1 mSv). As it is well known, dose limits do not apply to the medical exposure of patients, However, considering the magnitude of the patient exposures, the implementation of Dose Optimization and other Radiation Protection principles calls for appropriate clinical practices in view of the patient protection and safety.

The author recognizes and acknowledges that in all the medical institutions visited, there is awareness of the professionals towards Radiation Protection principles, namely optimization and dose reduction. Eventual flaws in the implementation of good practices are associated with each individual's awareness and methodologies and for this reason, the author believes that continuous education and training of workers that must deserve appropriate consideration from the individuals and from the managers.

The author hopes that the present work will contribute for a better understanding of the Portuguese reality in the Radiation Protection panorama, where the medical applications of ionizing radiation are concerned. She believes that the competences acquired during the execution of this Project greatly contributed to improve and enhance her perception of the responsibilities of the different professional groups within Radiological and Nuclear Medicine departments (physicians, medical physicists, radiographers and NM technologists, nurses and engineers). The possibility of visiting different medical institutions, as well as the discussion of practical aspects and implementation of the Radiation Protection principles (focusing on Dose Optimization) with experienced professionals, has been very beneficial to her knowledge and skills about medical imaging and medical applications of ionizing radiation.

7. Future Perspectives

Possible future work regarding Dose Optimization in Portuguese medical institutions might include, in CT, a prospective optimization study, where new protocols ought to be developed and implemented for the new CT scanners in use and the ones to be installed in a near future. As this work briefly addressed the problems in retrieving patient dose registry data, perhaps a more thorough, CT dose assessment-oriented study could evaluate the performance of several databases of CT procedures existing in different hospitals. These systems should provide an easy and direct access to the CT acquisition parameters, and smooth the easiness of estimating patient doses.

New research, within Nuclear Medicine institutions, should be centered on the actual estimation of patient doses, considering the administered activities and computational simulations of the biokinetics of incorporated radiopharmaceuticals. In this work, only the implemented Dose Optimization and Radiation Protection practices were evaluated, but a better understanding of the actual doses diagnostic patients are exposed to is equally important. In what concerns the professionals exposed, a very interesting study would involve the assessment of individual doses received per task, and the contribution of each task for the annual dose received by workers, in different institutions.

8. References

[1] Matanoski GM, Boice JD, et al. Radiation Exposure and Cancer: Case Study. AJE 2001; Vol. 154, No. 12.

[2] ICRP. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103 (March, 2007).

[3] BEIR. Health Risks from Exposure to Low Levels of Ionizing Radiation. BEIR VII Report (June, 2005).

[4] CSPH. Ionizing Radiation Exposure in the Medical Setting. Report 2 (A-06) (June, 2006).

[5] Hatch M, Drozdovitch V. NCI Studies of Health Effects Following the Chornobyl Nuclear Accident: What We Have Learned. Health Physics News 2008; Vol. XXXVI, No.5.

[6] Mettler FA, Huda W, et al. Effective Doses in Radiology and Diagnostic Nuclear Medicine: A Catalog. Radiology (2008); Vol. 248, No.1.

[7] NCRP. Medical Radiation Exposure of the U.S. Population Greatly Increased Since the Early 1980s. NCRP Report No. 160 (Press Release); 2009 Mar 2-3.

[8] NCRP. Report No. 160, Ionizing Radiation [Poster]. Available from: http://www.ncrponline.org/PDFs/Poster.pdf.

[9] WHO. Global Initiative on Radiation Safety in Healthcare Settings [Technical Meeting Report]. 2008 Dec 15-17, WHO Headquarters, Geneva.

[10] Jadvar H. Expanding Applications for PET and PET/CT Scanning. Medscape Radiology [Internet]. 2007 Mar [cited 2010 Out 18]. Available from: http://www.medscape.org/viewarticle/553465.

[11] Etard C, et al. Exposition de la population française aux rayonnements ionisants liée aux actes de diagnostic médical en 2007. IRSN Rapport, 2007.

[12] Council Directive 97/43/EURATOM (June 30, 1997).

[13] European Commission. European Guidance on Estimating Population Doses from Medical X-Ray Procedures; Annex 2 - Dose Datamed Report 1a. Radiation Protection No. 154 (2008).

[14] Medeiros J. Qualidade de Imagem versus Dose em Tomografia Computorizada – Optimização dos Protocolos de Crânio [thesis submitted for the degree of Master in Biomedical Engineering]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra; 2009.

[15] Powsner RA, Powsner ER. Essential Nuclear Medicine Physics, 2nd Edition. Blackwell Publishing; 2006.

[16] Botelho F. Interacções das Radiações com a Matéria [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2009.

[17] Bernardes R. Dosimetria da Radiação e Radioprotecção [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2009.

[18] Bodansky D. Nuclear Energy – Principles, Practices and Prospects, 2nd Edition. Chapter 4. New York: Springer, 2004.

[19] Botelho F. Efeitos Crónicos da Radiação [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2009.

[20] IAEA. Chapter 14 – Basic Radiobiology [Internet, cited Fev 2011]. Available from: http://www-naweb.iaea.org/nahu/dmrp/pdf_files/Chapter14.pdf.

[21] ATSDR. Principles of Ionizing Radiation [updated 2008 July 15; cited 2011 April 28]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp149-c2.pdf.

[22] Botelho F. Efeitos celulares da radiação [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2009.

[23] The History of Biology [Presentation on the Internet, cited Fev 2011]. Available from [Website main page]: keiserstudents.tripod.com.

[24] Botelho F. Radiobiologia [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2009.

[25] IAEA. Radiation Protection in Nuclear Medicine [Internet, cited Fev 2011]. Available from the website (main page): http://www.rpop.iaea.org.

[26] Cameron J. Radiation Dosimetry. Environmental Health Perspectives 1991; Vol. 91.

[27] Botelho F. Grandezas, Quantidades e Unidades usadas em protecção contra as radiações [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2009.

[28] Radiation Protection - Health Physics Technician Fundamentals Course [Internet, cited Apr 2011]. Available at: http://www.nukeworker.com/study/hp/neu/Part_2_Radiation_Protection/RP-4_Radiation_Protection.pdf.

[29] Shapiro J. Radiation Protection – a Guide for Scientists, Regulators and Physicians, 4th Edition. Harvard College, 2002.

[30] Principals of Radiation Protection [Internet, cited April 2011]. Available from: www.ehs.unr.edu/Documents/RadSafetyPrinciples.pdf.

[31] USNRC. Biological Effects of Radiation - Fact Sheet [Internet, cited Apr 2011]. Available from: http://www.nrc.gov/reading-rm/doc-collections/fact-sheets/bio-effects-radiation.pdf.

[32] ICRP. Statement on Tissue Reactions (approved April 21, 2011).

[33] Hendee WR, Ritenour ER. Medical Imaging Physics, 4th Edition. 2002 Wiley-Liss, New York.

[34] IAEA. Introduction to Radiation Protection in PET-CT [Presentation on the Internet, cited Jun 2011].

Available from the website (main page): http://www.rpop.iaea.org.

[35] Flohr T, Ohnesorge B. Multi-slice Technology. In book: Multi-slice and Dual-source CT in Cardiac Imaging (Part 3:41-69). Springer, 2007.

[36] Hounsfield GN. Computerized Transverse Axial Scanning (tomography): Part 1 – Description of the System. Br J Radiol (1973), 46:1016-1022.

[37] Policy implications of CT Scanner: An Update [Background Paper]. Jan 1981.

[38] SIEMENS AG, Medical Solutions. Computed Tomography – Its History and Technology.

[39] ACR. Practice Guideline for Performing and Interpreting Diagnostic CT (2006).

[40] FDA. Radiation-emitting products: CT [Website, last updated Set 2010, cited Mar 2011]. Available from: http://www.fda.gov/Radiation-EmittingProducts/RadiationEmittingProductsandProcedures/MedicalImaging/MedicalX-Rays/ucm115317.htm.

[41] American College of Radiology (ACR) and American Society of Neuroradiology (ASNR). Practice Guideline for the Performance of Computed Tomography of the Brain (2010).

[42] Suetens P. Fundamentals of Medical Imaging, 2nd Edition. Cambridge University Press, USA, 2009.

[43] Järvinen H. OPTIMEDI - Dose Optimization from New Technologies in Medical Imaging [Collaborative Project, unpublished version], 2010.

[44] Lima, JP. Tomografia Computorizada [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2010.

[45] Computed Tomography Systems and Subsystems (Website, cited Aug 2011). Available from: http://www.analogic.com/products-medical-computer-tomography.htm.

[46] GE Healthcare. GE Discovery™ PET/CT 600 - Learning and Reference Guide [Manual], 2009.

[47] Reddinger WL. CT Physics and Instrumentation [Presentation], 1997.

[48] McNitt-Gray MF. Tradeoffs in CT Image Quality and Dose. David Geffen School of Medicine, UCLA [Internet, cited Abr 2011]. Available from: http://www.oucom.ohiou.edu/ou-microct/Downloads/Tradeoffs_in_CT_Image_Quality_and_Dose_9794-13379.pdf.

[49] Breiki G et al. Evaluation of Radiation Dose and Image Quality for Patients Undergoing Computed Tomography Examinations. In: IX Radiation Physics & Protection Conference. 2008 Nov 15-1, Cairo, Egypt.

[50] Catalano C et al. Optimizing Radiation Dose and Image Quality. Eur Radiol Suppl (2007) 17 [Suppl 6]: F26-F32.

[51] KIM S et al. Computed Tomography Dose Index and Dose-Length Product for Cone-Beam CT: Monte Carlo Simulations of a Commercial System. J of App Clin Med Physics 2011; Vol. 12, No. 2.

[52] MORI S et al. Conversion Factor for CT Dosimetry to Assess Patient Dose Using a 256-slice CT Scanner. Br J Radiol 2006; 79:888-892.

[53] Stabin M. Nuclear Medicine Dosimetry. Phys. Med. Biol. 51 (2006) R187–R202.

[54] McGoron AJ. Radioisotopes in Nuclear Medicine. Florida International University, USA.

[55] Shyn PB. Newsletter PET-CT. Radiology Associates of Tarrant County. Volume 7, 2003.

[56] Townsend DW. Combined PET/CT: the historical perspective. University of Tennessee Graduate School of Medicine.

[57] WNA. Radioisotopes in Medicine [Website, updated Feb 2010, cited Fev 2011]. Available from: www.world-nuclear.org/info/inf55.html.

[58] Wilson BG. The evolution of PET-CT. Radiologic Technology (March-April, 2005).

[59] Chepel V. Imagiologia com Radioisótopos – Parte II: Tomografia com Emissão de Positrões [Presentation]. Faculdade de Ciências e Tecnologia da Universidade de Coimbra, 2010.

[60] Table of Radionuclides [Internet document, cited Jul 2011]. Available from: www.world-nuclear.org/info/inf55.html.

[61] Turkington TG. Introduction to PET Instrumentation. J Nucl Med Technol 2001; Vol. 29, No. 1.

[62] Schulthess GV. Pet/CT: Principles and Practices [Internet, cited Jul 2011]. University Hospital, Zürich, Switzerland, 2004. Available from: http://www.c2i2.org/summer2004/pet-ct%20principles%20and%20practices.asp.

[63] Medical Physics Consultants, Inc. Suggested Prescribed Dosage List, 2008.

[64] Guidance Levels of Dose, Dose Rate and Activity for Medical Exposure [on the Internet, cited Jul 2011]. Availbale from: http://www-pub.iaea.org/MTCD/publications/PDF/ss-115-web/Pub996_web-5.pdf.

[65] ICRP. Diagnostic Reference Levels in Medical Imaging: Review and Additional Advice [on the Internet, cited Jul 2011]. Available from: http://www.icrp.org/docs/DRL_for_web.pdf.

[66] EANM. Dosage Card [on the Internet, cited May 2011]. Available from: http://www.eanm.org/committees/dosimetry/dosagecard.pdf.

[67] Amaral A, Itié C, Bok B. Dose Absorbed by Technologists in Positron Emission Tomography Procedures with FDG. Braz Arch B Technology, Vol.50, Special Number : pp.129-134, September 2007.

[68] Mountford PJ, O'Doherty MJ. Exposure of Critical Groups to Nuclear Medicine Patients. Applied Radiation and Isotopes 50 (1999) 89±111.

[69] Harding LK, et al. The radiation dose to accompanying nurses, relatives and other patients in a nuclear medicine department waiting room. Nucl. Med. Commun. 11,17±22.

[70] Wahl RL. Why Nearly All PET of Abdominal and Pelvic Cancers Will Be Performed as PET/CT. 2004 J Nucl Med, Vol. 45, No. 1 (Suppl).

[71] IAEA. Radiation Protection of Patients PET-CT Scanning [Webpage, cited Apr 2011]. Available from: https://rpop.iaea.org/RPOP/RPoP/Content/InformationFor/HealthProfessionals/6_OtherClinicalSpecialities/PETCTscan.ht.

[72] Alessio AM, Kinahan PE, Cheng PM. PET/CT scanner instrumentation, challenges, and solutions. Radiol Clin N Am 42 (2004) 1017 – 1032.

[73] Sureshbabu W, Mawlawi O. PET/CT Imaging Artifacts. J Nucl Med Technol 2005; 33:156–161.

[74] Alessio A. PET/CT Instrumentation Basics [Presentation]. University if Washington, Nov 2007.

[75] Wang XA. CT Attenuation Correction in PET/CT Image Fusion [Project]. University of Texas, 2010.

[76] Khamwan K, Krisanachinda A, Pasawang P. The Determination of Patient Dose from 18F-FDG PET/CT Examinations. Rad P Dosimetry (2010), Vol. 141, No. 1, pp. 50-55.

[77] IAEA. Training Material on Radiation Protection in Nuclear Medicine, Part 12 - Protection of the General Public [Internet, cited Aug 2011]. Available from: https://rpop.iaea.org/rpop/rpop/content/additionalresources/training/1_trainingmaterial/index.htm.

[78] Reiman RE. PET Radiation Safety [Internet, cited Aug 2011]. Academy of Molecular Imaging, Duke university Medical Center. Available from: www.safety.duke.edu/radsafety/slides/pet_rad_safe.pps.

[79] Diário da República, Decreto-Lei nº 180/2002, No. 182 I-A (August 8, 2002).

[80] Brix G, Lechel U, et al. Radiation Exposure of Patients Undergoing Whole-Body Dual-Modality 18F-FDG PET/CT Examinations. J Nucl Med 2005; 46:608-613.

[81] Confédération Suisse. Niveaux de référence diagnostiques en tomodensitométrie [Notice]. Unité de direction Protection des consommateurs, 2010.

[82] SIEMENS. Dose Parameters and Advanced Dose Management on SOMATOM Scanners (White Paper). Siemens Medical Solutions USA (January, 2011).

[83] Pages J, Buls N, Osteaux M. CT doses in children: a multicentre study. Br J Radiol 2003; 76:803-811.

[84] Stern SH, et al. 2000-01 Survey of Patient Radiation Exposure from CT Examinations in the US. In: the 87th Scientific Assembly and Annual Meeting of the Radiological Society of North America. 2001 Nov 25-30, Chicago.

[85] ACR. CT Accreditation Phantom Instructions (2010).

[86] Hara N, et al. Assessment of Patient Exposure to X-Radiation from SPECT/CT Scanners. 2010 J Nucl Med Technol, Vol. 38, No. 3; 138-148.

[87] How to Develop CT Protocols for Children [Internet, cited Aug 2011]. Available from: http://www.bonepit.com/Reference/Protocols/CT%20children%20image%20gently.htm.

[88] ACR. CT Accreditation Program (2011) [Internet, cited Aug 2011]. Available from:http://www.acr.org/accreditation/computed/ct_reqs.aspx.

[89] Martin, MC. PET/CT – Site Planning and Shielding Design. In: National Symposium on Fusion Imaging and Multimodalities: Technical and Regulatory Considerations; 2004 Fev 18-20; Kansas City, Kansas.

[90] Diário da República, Decreto-Lei nº 222/2008, No. 223 I (November 17, 2008).

[91] Council Directive 96/29/EURATOM (May 13, 1996).

[92] Release of Patients Administered Radioactive Materials, USNRC Regulatory Guide 8.39 (April 1997).

[93] IAEA. L06 - Radiation Protection of Children during CT [Internet, cited Jun 2011]. Available from: http://rpop.iaea.org/RPOP/RPoP/Content/Documents/TrainingPaediatricRadiology/Lectures/PAEDIATRIC-L06-radiation-protection-of-children-in-ct.ppt.

9. Appendices

9.1. Appendix I. Nuclear Medicine and PET/CT Dose Optimization Questionnaire

1. Nuclear Medicine Facility general features

1.1. Professionals contacted to complete the survey (technologist, physicist, others): _____

1.2. Facility's location: _____

1.3. The department/facility is part of a:

a) Public institution
b) Private hospital

1.4. The department/facility is part of a:

a) Multidisciplinary center
b) Dedicated Nuclear Medicine center

1.5. Is radiopharmaceutical therapy (with patient internment) performed in the institution?

1.6. Number of therapeutic rooms (in the case of extended radiopharmaceutical therapy): __

1.7. Are the different rooms and areas in the Nuclear Medicine department organized by increasing level of activity?

1.8. Are area radiation levels monitored?

1.9. The drain-pipes from the injected patient's toilet room:

a) End up in a delay tank
b) Separate liquid radioactive waste, which ends up in a delay tank, from other virtually non-radioactive waste, which ends up in the main sewer
c) Go directly to the main building sewer, as it isn't mandatory for diagnostic-dedicated facilities to include delay tanks in their plumbing system

1.10. Number of Nuclear Medicine imaging in the institution:

a) __ Gamma-cameras
b) __ PET/CT scanners
c) __ Bone densitometers
d) Other Nuclear Medicine imaging equipments: _____

1.11. Imaging equipment's vendor:

a) GE Healthcare
b) Philips Healthcare
c) Siemens Healthcare

1.12. Most frequent diagnostic indications (both conventional Nuclear Medicine and PET/CT):

a) Oncology
b) Cardiology
c) Nephrology
d) Rheumatology
e) Others

1.13. Number (average) of daily performed examinations:

a) __ Conventional Nuclear Medicine examinations
b) __ PET/CT examinations

1.14. Average percentage of total pediatric examinations: __

1.15. γ-ray (conventional Nuclear Medicine) radionuclides used in the institution:

a) ^{99m}Tc
b) ^{123}I and/or ^{131}I
c) ^{111}In
d) ^{67}Ga
e) Others

1.16. β^+ (PET) radionuclides used in the institution:

a) ^{18}F-FDG
b) Other ^{18}F-labelled compounds
c) Others

1.17. Source of PET tracers: _____

2. Patient Preparation and Dose Optimization Procedures

2.1. In general, for all types of examinations (depending on the radiopharmaceutical used):

2.1.1. Which recommendations are normally given to the patient, while he/she awaits for the examination, after the radiopharmaceutical has been administered?

2.1.2. Which parameters are taken into account in determining the activity to be administered?

2.1.3. How are the radiopharmaceuticals administered (IV injection, ingestion, inhalation)?

2.1.4. Which patient levels are measured before radiopharmaceutical administration and during the examination (for different types of examination)?

2.1.5. Frequent dietary and pharmacological requirements before examinations (depending on the examination)?

2.1.6. Frequent administered drugs (depending on the examination)?

2.1.7. Is the patient's medical history previously assessed (does the patient consult the department's medical physician before the examination)?

2.2. Specifically for PET examinations, using ^{18}F-FDG:

2.2.1. Average FDG uptake period: __ min

2.2.2. Is blood glucose level measured before injection?

2.2.3. Average whole-body examination duration: __ min

3. Personnel Dose Optimization Procedures

3.1. Types of dosimeters used by the professionals: _____

3.2. Do technologists ever exceed the established dose limits?

3.3. On which situations are the technologists most exposed to ionizing radiation?

3.4. Which procedures are implemented in order to reduce exposure?

3.5. Who administers the radiopharmaceutical to the patient? Nurse/Technologist

3.6. Which shielding physical barriers are used?

3.7. Course of action when a worker's pregnancy is first known?

3.8. Are technologists regularly monitored for eventual contaminations?

3.9. Are area and personnel contaminations/accidents properly registered?

4. Members-of-the-Public Dose Optimization Procedures

4.1. Which indications, concerning close contact to other people after abandoning the facility, are usually given to the injected patient?

4.2. In the case of pediatric (or other) patients who need the company of a family member during the examination, which procedures are normally implemented?

4.3. Are the injected patients isolated from members of the public, when awaiting for their examination?

4.4. Is radiation exposure controlled for every student, or other "visitors" who remain inside the facility for some time (at least a few hours)?

9.2. Appendix II. Information on the DRLs and p75 calculations

1. About the Swiss DRLs

Both the adult and the pediatric DRLs were established based on Swiss studies and reports on patient dose [81]. The dose phantom used for the establishment of the reference values was a head phantom (160 mm diameter), in the [0], [1-5] and [6-10] age intervals in chest and abdomen examinations and in all head procedures, regardless of the age group. For the two older age groups ([11-15] and [16+]), a body phantom (320 mm diameter) was used.

2. Number of examinations of the studied $CTDI_{vol}$ distributions, on each age group

Age Group	HEAD		CHEST		ABDOMEN	
	H1	**H2**	**H1**	**H2**	**H1**	**H2**
[0]	38	10	2	2	1	0
[1-5]	92	38	7	19	2	2
[6-10]	86	60	6	16	4	7
[11-15]	103	78	12	39	5	12
[16+]	36	106	106	54	37	218

9.3. Appendix III. Information on the performed CT examinations

1. CT Equipments used

- "Portuguese Hospital 1" (H1) – single-slice detector
- "Portuguese Hospital 2" (H2) – multi-slice detector (64 slices)
- "Belgian Hospital 1" (B1) – single-slice detector
- "Belgian Hospital 2" (B2) – single-slice detector
- "Belgian Hospital 3" (B3) – multi-slice detector
- "American Survey" (A) – several different equipments, both single- and multi-slice

2. Protocols in use

- H1 – age-adapted protocol (in pediatric examinations)
- H2 – unkown/not available
- B1 – age-adapted protocol (in pediatric examinations)
- B2 – age-adapted protocol (in pediatric examinations)
- B3 – age-adapted protocol, (in pediatric examinations)
- A – unkown/not available

3. **Selected Technical Settings**

- Pediatric head examinations (depicted on Figure 4.13):

	H1 (mean values)	H2 (mean values)	B1	B2	B3
1 y-old	121 kV 112 mA Pitch = 1	114 kV Thick.: 1,1 mm Rot. Time: 0,9 s	120 kV 225 mA·s Thick.: 2/5 mm Table F.: 5/7 mm	120 kV 75 mA·s Thick.: 8 mm Table F.: 8 mm	120 kV 110 mA·s Thick.: 10 mm Table F.: 10 mm
5 y-old	122 kV 145 mA Pitch = 1	120 kV Thick.: 1,2 mm Rot. Time: 1,1 s	120 kV 225 mA·s Thick.: 2/5 mm Table F.: 5/7 mm	120 kV 75 mA·s Thick.: 8 mm Table F.: 8 mm	120 kV 160 mA·s Thick.: 10 mm Table F.: 10 mm
10 y-old	121 kV 162 mA Pitch = 1	117 kV Thick.: 1,1 mm Rot. Time: 1,1 s	120 kV 225 mA·s Thick.: 2/5 mm Table F.: 5/7 mm	140 kV 257 mA·s Thick.: 2/8 mm Table F.: 3/8 mm	120 kV 260-300 mA·s Thick.: 4/10 mm Table F.: 4/10 mm

- Adult head examinations (depicted on Figure 4.14):

H1 (mean values)	H2 (mean values)	A (mean values)
120 kV 195 mA Pitch = 1	120 kV Thick.: 1,2 mm Rot. Time: 2,0 s	127 kV 189 mA Rot. Time: 2,0 s 355 mA·s Thick.: 4,5-8,2 mm (narrow-wide)

4. **Number of examinations considered in this study**

- Pediatric head examinations (depicted on Figure 4.13):

	H1	H2	B1	B2	B3
1 y-old	35	7	N.A.	N.A.	N.A.
5 y-old	11	14	N.A.	N.A.	N.A.
10 y-old	22	18	N.A.	N.A.	N.A.

- Adult head examinations (depicted on Figure 4.14):

H1	H2	A
4	76	45