# Development of a Quality Assurance Program and

# Safety in Nuclear Medicine from the IAEA to the European Commission

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Masters in Medical Physics
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# Resumo

O programa de garantia de qualidade na Medicina Nuclear é indispensável dada a sua relevância na melhoria de cuidados dos pacientes bem como garantir a proteção dos trabalhadores e pacientes contra radiações ionizantes. A implementação dum programa de Garantia de Qualidade e Segurança nos serviços de Medicina Nuclear, de acordo com padrões internacionais como os da Agência Internacional de Energia Atómica (AIEA), Comissão Europeia (EC), Comissão Internacional de Proteção Radiológica (CIPR), garante que todos os procedimentos implementados e realizados num serviço de Medicina Nuclear, radiações ionizantes para exposições médicas, para fins diagnósticos ou terapêuticos, sejam controladas e otimizadas de acordo com padrões aceitáveis.

O presente trabalho tem como objetivo desenvolver um programa de Garantia de Qualidade e Segurança na Medicina Nuclear de acordo com as diretrizes e práticas recomendadas pela IAEA e pela Comissão Europeia, e também incluir a adaptação dessas diretrizes para a implementação prática em contextos clínicos variados focando na melhoria contínua da qualidade dos serviços e na segurança dos profissionais e doentes. Este programa pode ser também implementado em qualquer região, como o caso particular de Moçambique bastando para tal adequar as condições económicas e sociais à realidade do país. No programa desenvolvido, foram realizados vários testes de controlo de qualidade nos diferentes equipamentos usados no serviço de Medicina Nuclear do Instituto Português de Oncologia do Porto, a citar, teste de linearidade para calibrador de doses, uniformidade extrínseca e intrínseca, avaliação da sensibilidade e tempo morto para câmara gama e também foram realizados testes de quantificação no equipamento PET/CT usando 68Ga e 18F no âmbito da acreditação europeia de European Association for Research Limit (EARL/EANM).

No teste da linearidade de calibrador de doses, como o Capintec CRC-15R, opera dentro de uma determinada faixa onde existe uma relação linear entre as atividades esperadas e medidas. Vale ressaltar que alguns dados não apresentam linearidade, mesmo quando se considera o desvio entre as atividades esperadas e o modelo linear. Foi demonstrado que o calibrador de dose Capintec CRC-15R exibe linearidade em toda a faixa de 1,00E+02 a 1,00E+5 MBq. No caso do calibrador de doses Capinter CRC-15PET, a linearidade situa-se abaixo de 10 MBq, demostrando que é melhor do que o primeiro calibrador. De salientar que para ambos os calibradores de dose, foi medida uma atividade de 740 MBq de 99mTc, que é a atividade média para

uso clínico, o que nos permitiu fazer várias medições de queda de atividade em função do tempo ao longo de 5 dias até que a atividade atingir a atividade do fundo.

Quanto a uniformidades extrínseca e intrínseca da câmara gama, verificamos que os protocolos usados para os testes variam de fabricante para fabricante. Tendo sido desenvolvido um código em Python para análise dos dados obtidos. Este fornece resultados dentro de intervalos de tolerância, ou seja, fornece valores de uniformidade menores que 7%, respeitando os limites de aceitação presentes na legislação portuguesa. Os resultados foram também comparados com outros resultados utilizando o software ImageJ, assim como Plugins pré-existentes e disponíveis livremente.

No caso de sensibilidade das câmaras-gama, verificamos que a sensibilidade relativa entre os dois detetores, relativamente aos equipamentos Philips Brightview e Siemens Symbia pro.specta, difere em cerca de 5% e 1%, respectivamente. Além disso, câmara gama Philips Brightview possui um valor de sensibilidade relativamente baixo nos dois detetores quando comparado com o equipamento Siemens Symbia pro.specta. Isto acontece devido à natural diminuição da sensibilidade dos detetores ao logo do tempo.

Relativamente aos testes de quantificação PET/CT com 68Ga e 18F, foram adquiridas imagens, utilizando um fântoma de Jaszczak com atividades de 36,7 MBq e 70 MBq respetivamente, uniformemente distribuídas, com objectivo da obtenção da certificação EARL. Esta certificação garante que estudos adquiridos em diferentes equipamentos e diferentes centros sejam intercambiáveis e as informações de quantificação sejam comparáveis, sendo importante o estabelecimento de uma estratégia de harmonização da quantificação do SUV. Este teste é importante porque fornecendo informações quantitativas do metabolismo de glicose nos órgãos e os fatores que afetam o SUV como biomarcadores de imagens. Com isso, verificamos que o factor de calibração do equipamento PET corresponde ao factor de calibração do calibrador de doses.

**Palavras-chave:** Garantia de Qualidade, Segurança na Medicina Nuclear, Controlo de qualidade, Calibrador de doses, Câmaras-Gama.

# Abstract

A quality assurance program in Nuclear Medicine is essential due to its importance in improving patient care and ensuring the protection of workers and patients against ionizing radiation. Implementing a Quality and Safety Assurance program in Nuclear Medicine services, in accordance with international standards such as those of the International Atomic Energy Agency (IAEA), European Commission (EC), International Commission on Radiological Protection (ICRP), guarantees that all procedures involving ionizing radiation for medical exposure, whether for diagnostic or therapeutic purposes, are controlled and optimized according to acceptable standards.

The present work aims to develop a Quality and Safety Assurance program in Nuclear Medicine in accordance with the guidelines and practices recommended by the IAEA and the European Commission. This includes adapting these guidelines for practical implementation in varied clinical contexts focusing on continuous improvement in the quality of services and the safety of professionals and patients. This program can be implemented in any region, including Mozambique, by adapting to the country's economic and social conditions. In the program developed, several quality control tests were carried out on different equipment used in the Nuclear Medicine service of the Instituto Português de Oncologia do Porto. These tests included the linearity test for the dose calibrator, extrinsic and intrinsic uniformity, sensitivity assessment and the deadtime for the gamma camera. Additionally, quantification tests were performed on the PET/CT equipment using 68Ga and 18F within the scope of the European Association for Research Limit (EARL/EANM) European accreditation.

In dose calibrator linearity testing, the Capintec CRC-15R dose calibrator operates within a certain range where there is a linear relationship between expected and measured activities. It is worth mentioning that some data do not present linearity, even when considering the deviation between the expected activities and the linear model. The Capintec CRC-15R dose calibrator has been demonstrated to exhibit linearity over the entire range of 1.00E+02 to 1.00E+5 MBq. In the case of the Capinter CRC-15PET dose calibrator, the linearity starts below 10 MBq, demonstrating that it is better than the first calibrator. It should be noted that for both dose calibrators, an activity of 740 MBq of 99mTc was measured, which is the average activity for clinical use. This allowed us to make several measurements of the drop in activity as a function of time over 5 days until the activity reached the background level.

Regarding the extrinsic and intrinsic uniformities of the gamma camera, we found that the protocols used for testing vary from manufacturer to manufacturer. We have developed a Python code to analyze the data obtained, which provides results within tolerance bands. Specifically, it provides uniformity values lower than 7%, accordance with the acceptance limits specified in Portuguese legislation. The results were also compared with those obtained using ImageJ software, as well as pre-existing and freely available Plugins.

In the case of gamma camera sensitivity, we see that the relative sensitivity between the two detectors, in relation to the Philips Brightview and Siemens Symbia pro.specta equipment, differs by around 5% and 1%, respectively. Furthermore, the Philips Brightview gamma camera has a relatively low sensitivity value in both detectors when compared to the Siemens Symbia pro.specta equipment. This happens due to the natural decrease in the sensitivity of the detectors over time.

Regarding PET/CT quantification tests with 68Ga and 18F, images were acquired using a Jaszczak phantom with activities of 36.7 MBq and 70 MBq respectively, uniformly distributed, with the aim of obtaining EARL certification. This certification guarantees that studies acquired on different equipment and different centers are interchangeable and the quantification information is comparable, making it important to establish a strategy for harmonizing SUV quantification. This test is important because it provides quantitative information of glucose metabolism in organs and the factors that affect SUV as imaging biomarkers. With this, we verified that the calibration factor of the PET equipment corresponds to the calibration factor of the dose calibrator.

**Keywords:** Quality Assurance, Safety in Nuclear Medicine, Quality Control, Dose Calibrator, Gamma Chamber.

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| | |
|---|---|
| **EANM** | European Association of Nuclear Medicine |
| **EARL** | European Association for Research Limit |
| **EC** | European Commission |
| **ECDC** | Economic Cooperation and Development Communities |
| FCUP | Faculty of Sciences of the University of Porto |
| IAEA | International Atomic Energy Agency |
| ICRP | International Commission on Radiological Protection |
| IPO-PORTO | Instituto Português de Oncologia do Porto Francisco Gentil |
| NMS | Nuclear Medicine Service |
| NM | Nuclear Medicine |
| PET | Positron Emission Tomography |
| PET/CT | Positron Emission Tomography with Computed Tomography |
| SPECT | Single Photon Emission Computed Tomography |
| SPECT/CT | Single Photon Emission Computed Tomography /Computed Tomography |
| SUV | Standard Uptake Value |
| LOR | Line of response |
| UP | University of Porto |
| MPE | Medical Physics Expert |

# CHAPTER I

This chapter presents a brief overview of the contents to be covered in this work. It includes introduction, objectives, international framework of radiation, implantation of Nuclear Medicine service and structure of this work. These points are essential for a better understanding of the subsequent chapters.

## 1. Introduction

In recent years, the increase in oncological diseases has become more pronounced and constitutes a major threat to public health. According to the World Health Organization, it is estimated that there are 20 million new cases and 10 million deaths caused by cancer annually [1]. In Africa, particularly in underdeveloped countries such as Mozambique, cancer is considered the 3rd leading cause of death. It is classified as the 2nd cause of death in developed countries, including Portugal [2]. Several organizations and the scientific community have joined forces to mitigate this Public Health problem. One of the ways to combat cancer is by adopting new treatment techniques from diagnosis to therapy, using more precise ionizing radiation, such as Nuclear Medicine treatment [3].

To do that, it is necessary to implement a Quality and Safety Assurance program in nuclear medicine (NM) in accordance with international standards, such as those of the International Atomic Energy Agency, European Commission, International Commission for Radiological Protection. The Nuclear Medicine Quality and Safety Assurance program is based on guaranteeing and ensuring that all procedures implemented and carried out in a Nuclear Medicine service that uses ionizing radiation for medical exposures, whether for diagnostic or therapeutic purposes, are controlled and optimized in accordance with acceptable standards.

The International Atomic Energy Agency has developed several initiatives to improve Nuclear Medicine services oriented towards clinical application, aiming to improve clinical practices. These initiative includes Quality Management Audits in Nuclear Medicine practices [4], the Nuclear Medicine Resource Manual [5], General Safety Requirements in Nuclear Medicine (GSR part 1-3) on management systems for all facilities, Radiation protection and safety in medical uses of ionizing radiation (safety standards series Nº.SSG-46) among other documents aimed at clinical use and suggestions for implementing protocols [6]. Although IAEA, as a governmental and

international organization has consistently published standards and guidelines on the use of radioactive sources in Nuclear Medicine services, its guidelines have been widely implemented for developing countries, particularly in African countries, South America and Latin, and Asia. In contrast, they are and less implemented in the European Union and the United States of America due to the presence of another body such as the International Commission on Radiological Protection (ICRP).

The International Commission on Radiological Protection (ICRP), an independent private international organization [7], has developed research and recommendations on radiological protection structures from the professional perspective of using ionizing radiation for clinical purposes. This influence extends to the European Commission, which oversees the use of ionizing radiation in the region. Consequently, the European Commission has created such as Directive 96/29/EURATOM and Council Directive 2013/59/EURATOM, dated December 5, 2013 [3], which establishing for protection against the risks associated with exposure to ionizing radiation. The EC also publishes a Series of publications on radiological protection (RP-174, RP-162, RP-159, etc.). Since these Directives are mandatory within the European community, they suggest Guidelines and standards for the use of ionizing radiation at national and regional level. Both the IAEA and the EC emphasize the importance of establishing best practices for the use of ionizing radiation in Nuclear Medicine [8], based on the framework presented above, the objectives of the work are outlined below.

## 1.1. General objective

For its effective application, Nuclear Medicine requires a combination of different factors necessitating the implementation of quality assurance and safety programs across all dimensions to ensure clinical procedures meet internationally accepted standards. Instituto Português de Oncologia do Porto (IPO-Porto), the largest Oncology Center in the country, houses the Medical Physics, Radiobiology and Radiological Protection group, endeavours to implement and enhance various programs to ensure the quality of patient treatments in Nuclear Medicine services. Therefore, based on this overreaching objective, this work can be described as:

a) Development of a Quality Assurance Program and Safety in Nuclear Medicine from the IAEA to the European Commission

### 1.1.1. The main objectives

- A study of the IAEA and European Commission quality assurance criteria for Nuclear Medicine;
- Comparative analysis of IAEA and European Commission recommendations;
- Development of an integrated quality assurance and safety program model;
- Proposals for adapting the model for implementation in different demanding clinical contexts and with resource limitation;
- Assessment of the practical and theoretical implications of the proposed program
- Development of images quantification code: This code should automatically detect the images and analyze parameters such as intrinsic and extrinsic uniformity, deadtime.

## 1.2. Overall thesis structure

This thesis is divided into 6 chapters, namely: **Chapter I** which begins with a brief introduction, followed by objectives, Physical Principles of Nuclear Medicine, international framework of radiation, implantation of Nuclear Medicine service. **Chapter II** describes the IAEA Quality Assurance in Nuclear Medicine which will form the basis for understanding the overview of guidelines and protocols in Nuclear Medicine. **Chapter III** describes the European Commission Quality Assurance in Nuclear Medicine and discusses the quality assurance of nuclear medicine highlighting the General Principles of Radiological Protection in Nuclear Medicine. **Chapter IV** presents a comparative analysis made of the IAEA and EC recommendations on quality assurance in nuclear medicine as well as the current situation of Medical Physics in Mozambique. **Chapter V** presents the Practical implementation of the quality assurance program including some quality control tests, results and discussions. **Chapter VI** presents conclusions and future work, and finally bibliographical references are presented, followed by annexes.

## 1.3. Physical Principles of Nuclear Medicine

The physical principles underlying nuclear medicine are based on the use of radioactive substances for diagnosis and therapy. Radioactivity is a process in which an unstable nucleus transforms into a more stable one by emitting particles, photons, or both, and releasing energy in the process, causing the nucleus to always tend toward its lowest possible energy. Most nuclides found naturally on Earth today are stable, and more have been experimentally tested using accelerator or reactor facilities. It is estimated that of the more than 3300 nuclides studied, approximately 250 are stable, 90

are naturally occurring radionuclides, and 2960 are artificially generated radionuclides. Radioactive decay is considered spontaneous when the decay of a given nucleus cannot be predicted and is not significantly affected external events [9].

### i. Alfa-$\alpha$ decay

Alpha decay is a form of radioactive decay that occurs when an unstable atomic nucleus emits an alpha particle, transforming into another atomic nucleus with an atomic number two units smaller and a mass number four units smaller [10]. This decay process is more common for heavy (high-Z) unstable nuclei and is an efficient method of reducing their mass.

$$ {}^{A}_{Z}X \rightarrow {}^{A-4}_{Z-2}Y + \alpha \qquad \text{Equation 1.1.} $$

The alpha particle is the nucleus of a helium atom ($^{4}_{2}H_e$). Therefore, the alpha particle is a 2+ charge ion with two neutrons and two protons. Energy is released in the decay (the Q-value), which can be calculated as the difference in mass energy between the parent nucleus and final products, typically amounting to several MeV [10]. One such example is 223Ra which decays to Radon 219:

$$ {}^{223}_{88}Ra \rightarrow {}^{219}_{86}Rn + {}^{4}_{2}H_e. \qquad \text{Equation 1.2.} $$

Radium has similar chemical properties to calcium and is readily taken up by bones. This is one of the reasons why 223Ra is used in nuclear medicine for the treatment of metastatic bone cancer [11].

### ii. Beta-$\beta^-$ decay

In β− decay, a neutron is converted into a proton, with the emission of an electron and an electron antineutrino (the antiparticle of the neutrino). Schematically, it can be represented by:

$$ n \rightarrow p + \beta^- + \bar{\nu} \qquad \text{Equation 1.3.} $$

The atomic mass-energy balance equation is:

$$ {}^{A}_{Z}X \rightarrow {}_{Z+1}{}^{A}Y + \beta^- + \bar{\nu} \qquad \text{Equation 1.4.} $$

The energy of a $\beta^-$particle when it is released varies from zero to the maximum decay energy. The energy that separates the parent and daughter nuclides is called the decay or transition energy. The difference between the decay energy and the energy of the $\beta^-$particle is carried away by an antineutrino [10]. If the daughter nuclide is in an excited state and the number of $\gamma$-rays emitted is dependent on the excitation energy, then $\gamma$-ray emission may occur after the $\beta^-$decay, depending on the excitation energy. The atomic number of the daughter nuclide after beta decay is one unit greater than that of the parent nuclide, but the mass numbers of both nuclides remain the same. [11].

It should be noted that $\beta$-particles can penetrate small thickness, travelling a short distance in human body. Consequently, they are not useful diagnostic imaging purposes and are difficult to detect by the detector after passing through the patient's body [9]. In contrast, the $\beta^-$particles are very useful in nuclear medicine therapy. It is important to note that, after the electron interacts with tissue, it slows down and can emit radiation that depends on the material, a process known as ***Bremsstrahlung.***

### iii. Beta-$\beta^+$ decay-Positron

Following the same conservation laws as in the situation ( $\beta^-$ decay), a positron ($\beta^+$) and neutrino ($v$) are emitted in $\beta^+$decay. The $\beta^+$decay process occurs in proton rich nuclei. In this case, it can be formulated that in $\beta^+$decay, a proton is converted into a neutron in the nucleus, with the emission of a positron and an electron neutrino:

$$ {}^{A}_{Z}X \rightarrow {}_{Z-1}{}^{A}Y + \beta^+ + v \qquad \text{Equation 1.5.} $$

The antiparticle of an electron is called a positron. It typically comes to rest a few millimeters from its origin in the human body after being emitted from the nucleus and losing kinetic energy through collisions with atoms of the surrounding material. Within a few picoseconds, the positron can form the positronium when it combines with an electron, creating a bound state where the positron acts as the nucleus. The positronium has lifetime of about $10^{-10}$ s. Consequently, the positron annihilates with an electron in an annihilation reaction. During this process, their masses are converted entirely into energy, as shown in figure 1.1. Each particle has a mass-energy equivalent of 0.511 MeV. This energy is released in the form of two 0.511 MeV photons, which are emitted in nearly exact opposite directions from the annihilation site [11].

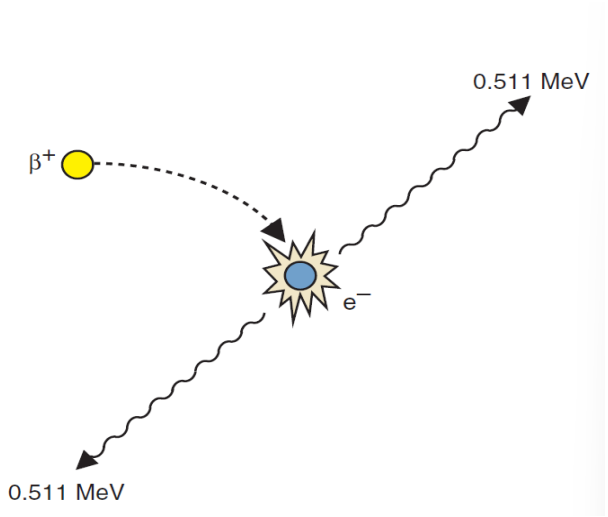


Figure 1.1. Schematic representation of mutual-annihilation reaction between a positron (β+) and an ordinary Electron [11].

The additional energy above 1.022 MeV in $\beta^+$ decay is shared by the neutrino and the positrons as their kinetic energy. The energy spectrum of positrons is comparable to that of $\beta^-$particles [10].

### iv. Electron capture

Electron capture, also called inverse $\beta^-$ decay is a process in which an orbital electron is captured by nucleus and combines with proton to form a neutron and emitting neutrino:

$$p^+ + e^- \rightarrow n + v \qquad \text{Equation 1.6.}$$

It is important to refer that the neutrino emitted in the process carries away most of the transition energy. The remaining energy appears in the form of characteristic x-rays and Auger electrons, which are emitted by the daughter product when the resulting orbital electron vacancy is filled [9]. Nevertheless, the electron is captured from orbits near to the nucleus known as K and L shells. Schematical can be represented as:

$$^A_Z X \rightarrow {}^A_{Z-1} Y \qquad \text{Equation 1.7.}$$

Note that, like $\beta^-$ decay it is an isobaric decay mode leading to a transmutation of elements. Electron capture decay is a consequence in a daughter nucleus that is in an excited or metastable state.

### v. Internal conversion

The internal conversion process involves the transfer of excitation energy from an excited nucleus to an orbital electron, preferably the K-shell electron, which is then ejected from the shell, creating a vacancy. This ejected electron is called the conversion electron [10]. The kinetic energy of the conversion electron is given by:

$$E_{IC} = E_{\gamma} - E_B, \qquad \text{Equation 1.8.}$$

where, $E_{\gamma}$ is the excitation energy and $E_B$ is the binding energy of the electron. Although *K*-shell electrons are more likely to be ejected due of their proximity to the nucleus, the electrons from the *L* shell, *M* shell, and beyond also may undergo the internal conversion process [12].

As vacancies created during internal conversion, there is a natural for electron in surrounding electronic shells to rearrange in order to fill these vacancies and achieve [13]. This filling process often involves the emission of X-rays or Auger electrons, can create new vacancies in the outer electron shells. [9].

### vi. Gamma-$\gamma$ ray Emission

Gamma rays is electromagnetic radiation that produced when a daughter nucleus passes from an excited level to a lower energy level by the emission of energy as gamma radiation. The energy of the $\gamma$-ray emitted is the difference between the two states upper energy levels and the lower energy levels [11]. Gamma rays from radioactive decay typically range in energy from a few kiloelectronvolts (keV) to approximately 8 MeV, corresponding to energy levels typically found in nuclei with relatively long lifetimes. Transitions that result in gamma emission leave Z and A unchanged and are called isomeric transition [14].

### vii. Radioactive decay law

Radioactive decay is a random process in which an unstable nucleus transforms into a more stable one, thus cannot be exactly predicted over time [15]. However, statistically, radioactive decay can be summarized as the decay of many nuclei in a sample observed over a certain period of time, using mathematical relationships to calculate the probability of decay [9]. Let us consider N as number of nuclei observed, the average decay rate is given by:

$$\frac{dN}{dt} = -\lambda N, \qquad \text{Equation 1.9.}$$

where $\lambda$ is the decay constant for the radionuclide. In some situations, it is possible that, the nucleus decays into more than one decay process. Thus, the decay constant is a sum of each contribution in the process [9]. Mathematically it is given by:

$$\lambda = \lambda_1 + \lambda_2 + \lambda_3 + \lambda_4 \ldots\ldots \lambda_n. \qquad \text{Equation 1.10.}$$

The negative term in equation (1.9) represents a loss of radioactive nuclei decay from the radioactive sample over time. Using concept of integration, the number of radioactive nuclei, N, can be written [9]:

$$N = N_0 e^{-\lambda t} \qquad \text{Equation 1.11.}$$

The equation 1.11 shows that, the number of radioactive nuclei, decays exponentially as a function of time [10]. Here, $N_0$ represents the initial number of radioactive nuclei. From equation 1.11, we can say that, activity is defined by:

$$A = \frac{dN}{dt} = -\lambda N \qquad \text{Equation 1.12.}$$

Note that, because activity *A* is proportional to the number of atoms *N,* the decay factor, also applies to activity versus time:

$$A = A_0 e^{-\lambda t} \qquad \text{Equation 1.13.}$$

Another parameter to consider is half-life ***(***$T_{1/2}$) which can be defined as the time required for half of the nuclei in a sample to decay. If the quantity that decays have a value at the beginning of the process [11], in the half-life the quantity will have half this value. Thus, half-life from equation 1.11 and substituting it by $N = N_0/2$ is given by:

$$\tau_{1/2} = \frac{ln2}{\lambda} \qquad \text{Equation 1.14.}$$

The uses of radionuclides as drug for diagnostic as well as treatment is involves another parameter called effective half-live, which is defined as the time required for a radionuclide in an organism to decrease its activity by half, considering biological elimination and radioactive decay (physically decay) [9]. Mathematically, it can be written:

$$\frac{1}{\tau_{eff}} = \frac{1}{\tau_b} + \frac{1}{\tau_p}, \qquad \text{Equation 1.15.}$$

where $\tau_b$ is the time required for an organism to remove, through biological elimination, half the amount of an administered substance, while $\tau_p$ is the physical half-life, characteristic for all radionuclides in terms of the time required for half of the radioactive nuclei to disintegrate [16].

During the radioactive decay process there is some fraction of activity that remains in the sample at any given time, what is called the decay factor (DF) [9]. The decay factor parameter can be calculated, dividing the number of nuclei for any time and the initial number of nuclei:

$$DF = \frac{N}{N_0} = e^{-\lambda t} \qquad \text{Equation 1.16.}$$

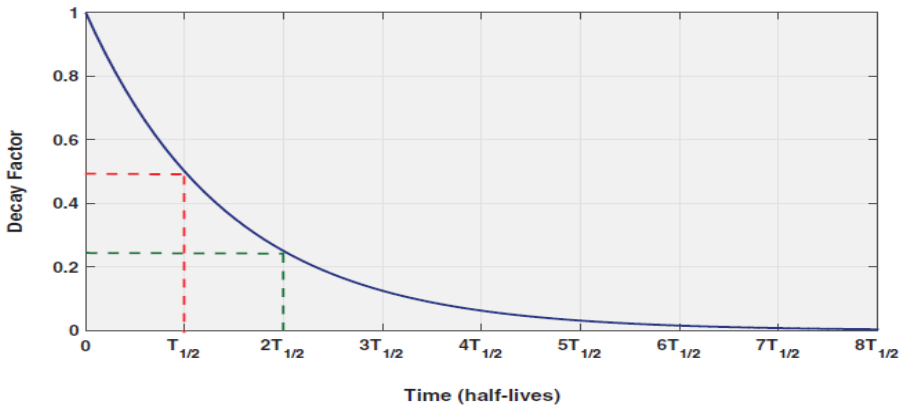


Figure 1.2. Decay factor as a function of time [9].

The half-life (and therefore decay constant) can be determined by experimentally, measuring the decay rate of a sample as a function of time. Two units of activity are widely adopted in nuclear medicine: Becquerel (Bq) the unit of radioactivity in the International System of Units (SI) and is defined as one nuclear disintegration per second, and Curie (Ci), a non-SI unit of radioactivity defined as $3.7\ x\ 10^{10}$ disintegrations per second.

## viii. Dose calibrator

Medicine is making great strides towards accurate diagnosis and treatment of diseases. The administration of a radiopharmaceutical for clinical use requires the use of sensitive instruments for detecting and measuring radioactive emissions known as a dose calibrator [17]. In nuclear medicine, the most used dose calibrator is composed of

an electrometer, in a sealed ionization chamber, in cylindrical shape, with a central well where the radioactive source is positioned along the longitudinal z-axis (see figure 1.13), and two electrodes with an applied potential difference [18].

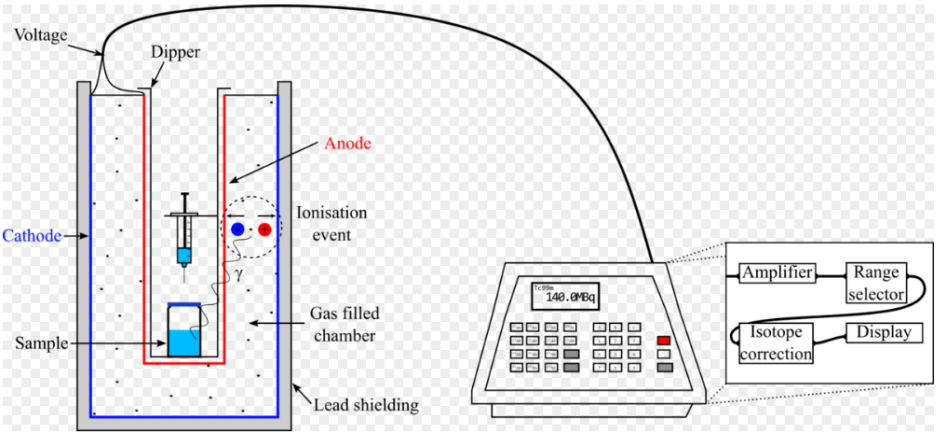


Figure 1.3. Representation of a dose calibrator [17].

Different activities produce different energy sources, resulting in the generation of different amounts of current. Its operating voltage is about 150 V. The ionization chamber is filled with argon gas at high pressures ranging from 5 to 12 atm [11]. Thus, the type of gas used, as well as its volume and pressure, influence the calibrator's response [18]. This highly compressed gas favours the possibility of ionizing events due to the ionic environment created. However, when a beam of radiation passes through the gas it causes the ionization of molecules forming pairs of ions, attracted to the anode (positive electrode) and the positive ions to the cathode (negative electrode), creating an electric current, see the figure 1.4.

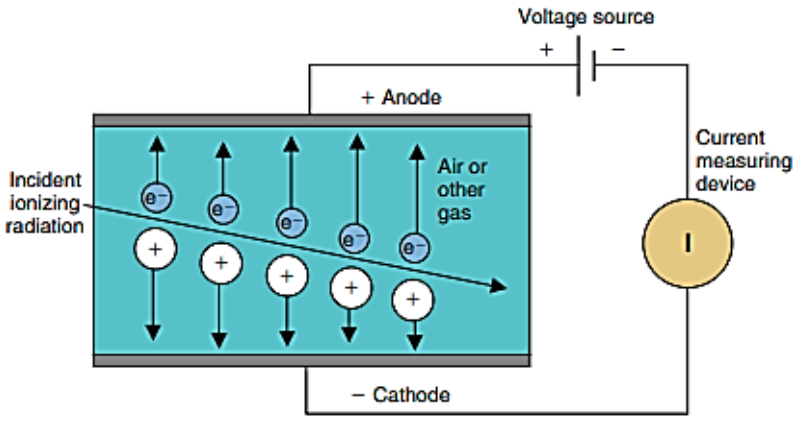


Figure 1.4. Gas-filled detector operation typical of ionization chambers [11].

To measure activity, it is necessary to define the calibration factor for the radionuclide. Then, the sample in a suitable container such as a syringe is placed into the dose calibrator chamber and the activity reading is displayed on the dose calibrator's digital meter [18].

### ix. Gamma camera

The gamma camera, also known as Anger camera, is a device used in nuclear medicine, developed to generate a planar, 2D-dimensional, or 3D-dimensional image of distribution of the radiopharmaceuticals administered to a patient [10]. It produces an image of the patient's organs with cold areas that emit few gamma rays and hot areas that, compared to the cold areas, emit many gamma rays. The gamma camera is composed of *collimator, larger area Thalium-doped Sodium Iodine (NaI(Tl)) scintillation crystal, a light guide and an array of photomultiplier tubs (PM)*. Figure 1.5 illustrates the basic principles of image formation with the gamma camera [11].

The collimator is made up of a dense material and a series of holes, allowing only radiation that propagates in a certain direction to pass through. Its purpose is to limit γ-rays that reach the detector with unwanted inclination. Thus, only the desired γ-rays reach the scintillation detector, forming an image projected onto the crystal surface [6].

The crystal (NaI(Tl)) absorbs γ-rays and converts them into visible light, which is collected by the light guide and directed to the photomultiplier tubes, where it is converted into amplified and processed electrical signals, allowing the location of each scintillation event to be determined and form a planar image [10].

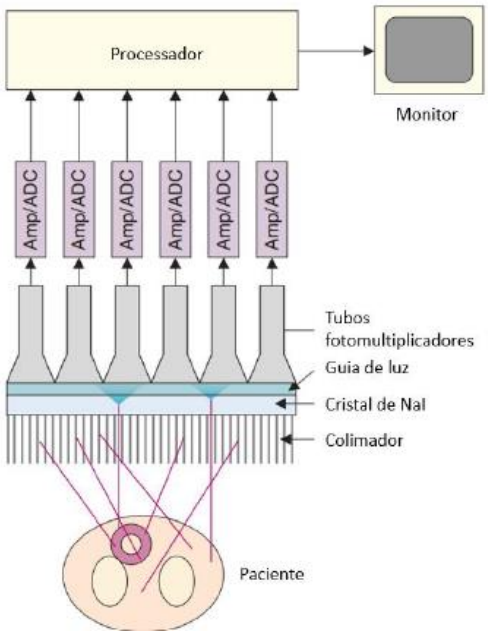


Figure 1.5. Basic principles and components of a modern gamma camera [11].

Although the gamma camera in terms of image quality, detection efficiency and ease of clinical use is similar to modern PET, it has limitations. The gamma camera imaging technique limitation is that the images obtained are two-dimensional (2D) projections of three-dimensional (3D) objects, which leads to an overlap of structures during image acquisition. One solution to this problem is to obtain images from different angles around the patient. To solve this problem, SPECT imaging is used as an alternative.

## x. Single photon emission computed tomography (SPECT)

The SPECT system is a tomographic medical imaging technique in nuclear medicine. It is the same as the gamma camera image and differs in image acquisition modes. It consists of a system with a gamma camera that rotates around the patient's body to acquire 3D images [19]. Therefore, 2D images are obtained at each projection angle, which, using mathematical image reconstruction algorithms, allows obtaining a 3-dimensional image, as seen in figure 1.6.

The image quality obtained by the SPECT system can be improved by incorporating more detectors. Currently, there are SPECT systems with up to three sets of detectors [11]. The advantage of these double and triple systems is that they allow two or three angular projections, respectively, to be acquired simultaneously [20].

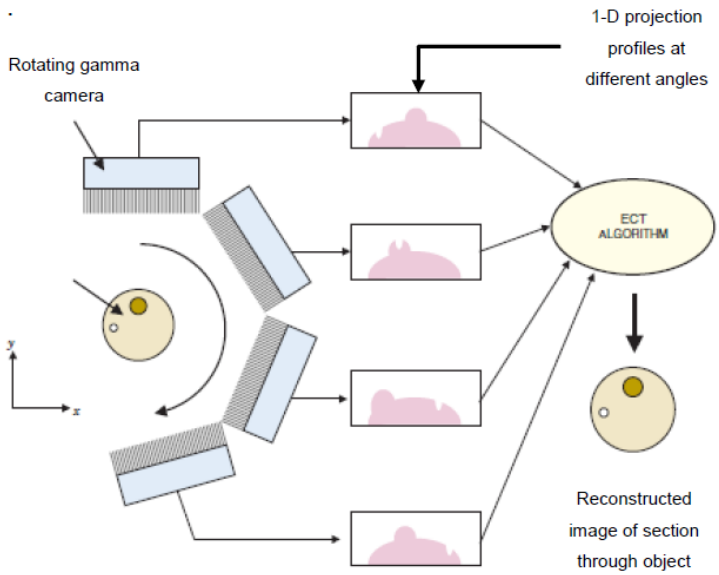


Figure 1.6. Representative scheme of SPECT image formation [19]

Thus, for the same acquisition time, the number of counts increases, increasing spatial resolution and image quality.

## xi. Positron Emission Tomography (PET)

The PET technique uses positron emitting radionuclides that, after being emitted, interact with electrons, forming the annihilation process that results in the emission of two photons in opposite directions with the same energies of 511 keV [11]. Thus, the two photons are detected, allowing the location where the emission and radioactive decay occurred to be determined. As previously mentioned, the PET system is made up of detectors that are distributed around the patient and when a pair of photons is emitted, they will be detected by two opposing detectors simultaneously [21], which allows the system to assign the photons to a line of response (LOR), as seen in figure 1.7.

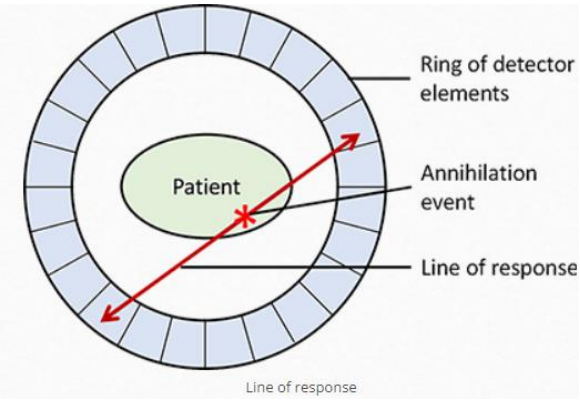


Figure 1.7. PET image acquisition [21].

The LOR is only assigned if photons are detected within the coincidence window, which typically corresponds to a time interval of 6 to 12 ns [11]. The PET system identifies real, scattered and random events, the latter of which impact the accuracy of PET images (Figure 1.8). Real events occur when 511 keV annihilation photons are detected at the coincidence time without undergoing any interaction before reaching the detector. On the other hand, random events occur when two distinct annihilation process photons are detected at the same time, allowing it to appear like a true coincidence [21]. This adds background to the actual coincidence event, increasing statistical noise and decreasing contrast. Finally, stray events occur when one or both annihilation photons undergo Compton interactions in body tissues, deviating from the expected route but still reaching the detectors [22].

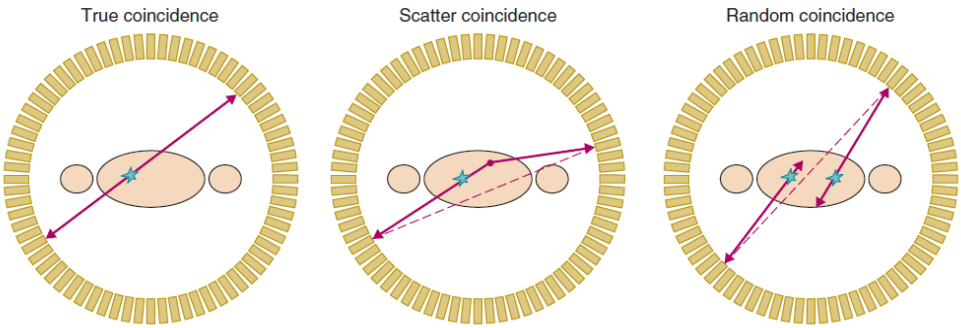


Figure 1.8. Type of events possible during the acquisition of a PET image [11].

The detectors used in PET are similar to those used in gamma cameras. They are scintillators that absorb photons emitted during annihilation processes and convert them into visible light. This light is then captured by photomultipliers and amplified into electrical signals. [10].

In the PET system, each detector is connected by a coincidence circuit to a series of opposite detectors. This circuit is responsible for letting pulses that are within the coincidence window (6-12ns) [11], pass to the opposite detector, rejecting pulses outside this window. The pulses detected within the coincidence window are processed through a circuit that combines both pulse signals, resulting in an output signal proportional to the total energy of the detected event. These signals are then amplified and processed further, enabling the determination of annihilation positions and the generation of an image showing the distribution of the radionuclide in the patient's body. [12].

The PET system operates in 2D or 3D mode. In the 2D acquisition mode, each detector has a septum that acts as a collimator, which blocks unwanted coincidence events due to Compton scattering [11]. Therefore, only photons emitted parallel to the detector plane are detected, see figure 1.9. By combining the images obtained in each plane, it is possible to obtain a reconstructed image.

Figure 1.9. Shows 2D image acquisition in PET [11].

A limitation in 2D imaging is that scattered photons are rejected and photons from true coincidence events are absorbed by the septa. In 3D acquisition, the septa are removed in such a way that all recorded response lines (see figure 1.8) increase sensitivity between 4 and 8 times. The absence of a collimator allows the recording of response lines resulting from random events to be increased [19]. Thus, the increase in sensitivity and the implementation of dispersion correction techniques make this acquisition modality the ideal mode of operation.

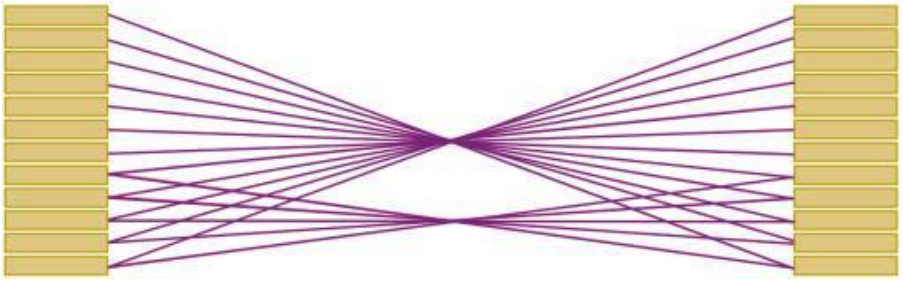

Figure 1.10. Representative scheme of 3D image acquisition in PET [11].

## xii. SPECT/CT and PET/CT

The SPECT and PET systems provide functional tissue information using radiopharmaceuticals that interact with specific molecules, allowing the evaluation of their physiology or metabolism. The only limitation of both techniques is that they do not provide anatomical information, which makes clinical decisions as well as the origin of this information difficult. However, the use of computed tomography (CT) allows obtaining anatomical information with excellent resolution. Hence the need to use combined SPECT/CT or PET/CT modalities.

Computed tomography is an imaging technique that uses X-rays to acquire images of the patient's interior. X-rays are produced in an X-ray tube like the one shown in figure 1.11. This tube consists of two electrodes, the cathode and the anode, which are under vacuum [23]. The cathode, which consists of a tungsten filament, emits electrons when passed through an electric current. The electrons, due to the high potential difference between the electrodes, are accelerated towards the anode.

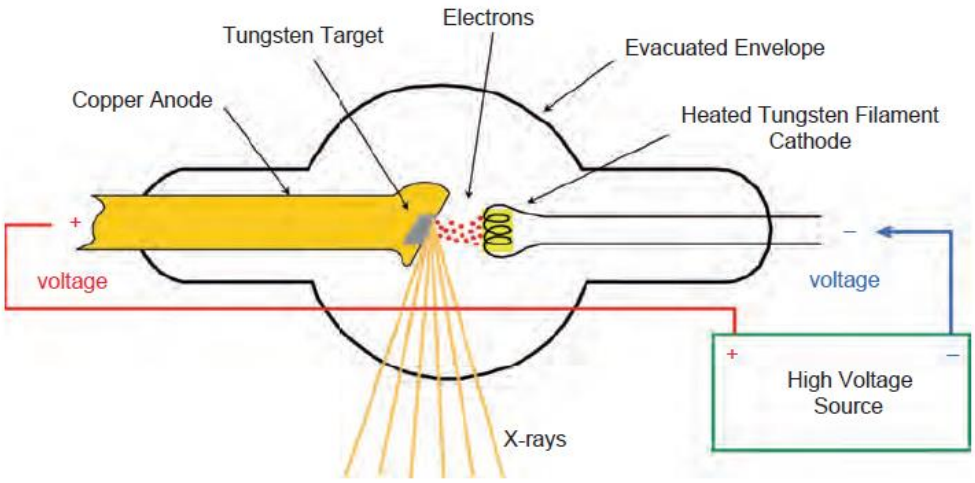


Figure 1.11. Shows the X-ray production tube, source and an electron target [24]

This interaction with the anode can occur in two distinct processes, namely the production of Bremsstrahlung radiation and characteristic X-rays. The first occurs when electrons approach the nuclei of the anode atoms and are attracted, resulting in a deceleration and change of direction. Consequently, they lose part of their kinetic energy, which is converted into Bremsstrahlung radiation [23].

The production of characteristic X-rays (see figure 1.12) occurs when the electrons in the less energetic layers of the anode atoms are knocked out of their orbit during the interaction with radiation, causing a gap. When electrons at higher energy levels fill the holes, they emit energy in the form of specific X-rays corresponding to the difference in the energies of the layers between which the electron passed [20]. Thus, the energy spectrum resulting from the production of X-rays has a set of well-defined peaks, which correspond to the characteristic X-ray photons, and a continuous part, which corresponds to the photons emitted through the Bremsstrahlung process [24].

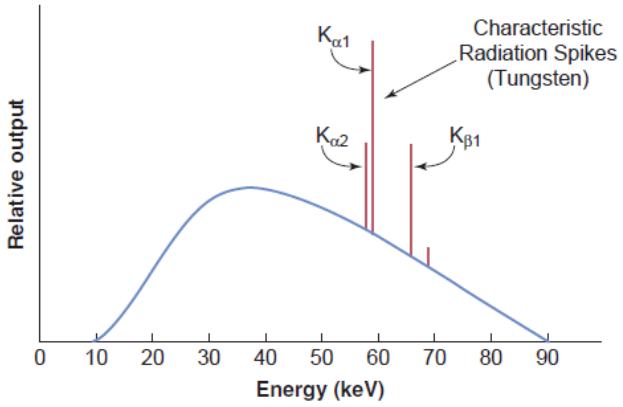


Figure 1.12. Energy spectrum of an X-ray bulb with tungsten anode [20].

In computerized tomography (CT), the x-ray tube assembly rotates around the patient, emitting an x-ray beam that passes through the patient. Thus, the information obtained provides images through several cross-sections of the patient.

## 1.4. International overview of radiation protection

In 1996, Antoine Becquerel discovered radioactivity emitted by uranium compounds and after two years later Marie Curie and Pierre isolated the radioactive particles of radium and polonium in which the first one was used for the treatment of cancer [16]. Although these particles explore huge medical benefits for diagnosis and therapy, has radiation-induction damage. The most obvious form of hazard resulting from ionizing radiation is radiation burns, since then, many efforts have been made focused on their prevention in practitioners than patients. It was because of these issues that gave rise to radiation protection [25]. Thus, the definition of radiation protection involves technologies and operations regarding to protection of human including patients, radiations workers, public members against the hazard and effects of the use of ionizing radiation.

Nowadays there are many scientific studies that aim to gradually reduce harmful radiation effects in human body in particular radiation induction cancer, for which there is always a certain risk even through at low doses of ionizing radiation and these risks cannot be eliminated [26]. Therefore, it is important to balance the benefits of nuclear medicine practices against radiation risk and efforts to minimize residual risk, this has been a huge challenge of radiation protection.

Ionizing radiation as well as radioactive substances are defined as natural characteristics of the environment, so-called natural radiation, namely cosmic rays, terrestrial gamma rays in particular uranium, thorium, potassium (40K), and radon decay products [16]. Thus, people are exposed to this radiation both externally and internally, through inhalation and ingestion. On the other hand, we have artificial radioactivity, which comes from nuclear weapons tests, also exposes people to radiation in the two forms mentioned above, although at much lower levels compared to natural radiation [27]. There are several agreements worldwide to reduce atmospheric exposure such as the 1963 treaty and the reduction of nuclear weapons programs. Figure 1.13 and 1.14, show that the majority of radiation dose to the population in the European Union and United States comes from natural sources 87% and 82% respectively [25], [28].

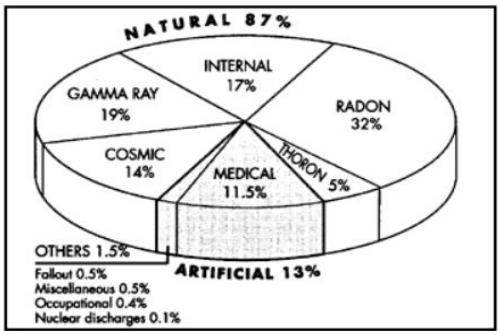


Figure 1.13. Dose contribution to individuals in the EU [25]

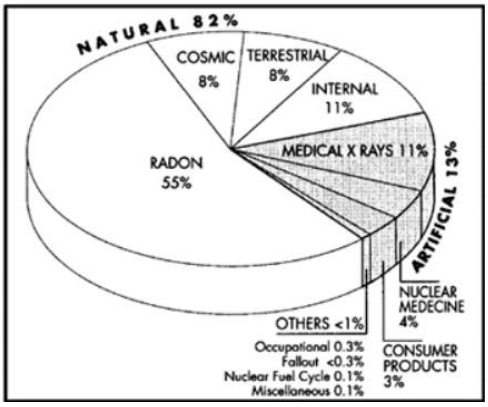


Figure 1.14. Dose contribution to individuals in the US [25]

The specific contribution of each source varies with factors such as altitude and medical use of radiation.

Human activities that result in increased exposure to natural radiation are called practices, while those that aim to minimize this exposure are called interventions [28]. In most cases, part of the exposure occurs under acceptable operating conditions, however, variations can result in potential exposures, which are generally uncertain and depend on several factors. It is important to note that radiological protection for practices is founded on 3 principles proposed [29] by the International Commission on Radiological Protection (ICRP), which can be presented:

1. ***Justification:*** regarding radiation practices exposure should be used only when benefits outweigh the harms, taking into account of economic and social factors.
2. ***Optimization:*** After justification, great care must be taken in its execution to minimize the risk of radiation, keeping doses as low as possible, without affecting clinical purposes and without excluding economic and social factors.

3. ***Limitation:*** the last justification regarding radiation exposure considers that the dose must be limited to ensure that unacceptable risks do not occur, and such limits must be very clear for the application of the principles of justification and optimization.

The intervention, on the other hand, is based on retroactive protection principles to minimize existing exposure due to accidents. It involves two principles namely:

1. **Justification:** the intervention must come at the expense of benefits, without leaving out social and economic costs**.**
2. **Optimization:** for best success, the intervention must be optimized to maximize the benefits of dose reduction, considering the social and economic costs involved.

Radiation protection is a challenge that dates back a long time since guidelines were first proposed in 1930 on the use of radioactive sources, whether natural or artificial, as cited by the International Commission on Radiation Protection (ICRP) [29].

## 1.5. Framework for radiation protection

As said referenced earlier, the first definition of radiation protection was suggested by ICRP, addressing the principle for operational procedures and guidance for nuclear Energy, medical exposure for diagnostic and therapy, and natural radiation later joined by other organization such as the European Commission (EC), International Atomic Energy Agency (IAEA), Nuclear Energy Agency (NEA), since then, all countries in the world incorporate ICRP definition in order to meet criteria and procedures for radiation protection in their practices.

There are requirements for establishing framework of radiation protection, which involves an effective infrastructure, laws and regulations, qualified human resources and an efficient regulatory system [29]. For successful implementation, it is desirable that all staff involved have an attitude and behavior regarding radiation protection duties beginning with workers, management levels that ensure that the safety culture is guaranteed [30].

The national legislation needs to meet all requirements as recommended by ICRP starting with authorization for registration and sources licensing, followed by inspection and enforcement actions [13]. Regulatory authority not only has powers, but also assumes responsibilities to the public for the performance of these tasks, and licensees are those who guarantee the safety of the sources that hold them and establish

safety within the organization by protecting workers, the public against radioactive sources [16].

An essential aspect of radiation protection principles linked to the infrastructure is ideal measurement devices, technology used to assess and software also qualified personnel [29]. The technology involved in this case will continue with improvements in devices over time including their method and control according to the development of electronics equipment and nuclear industries [28]. Regarding the quality of radiation protection buildings, there are a lot of situations in the world.

Many studies have demonstrated that the Economic Cooperation and Development Communities (ECDC) which Portugal is a member have well-established buildings in the field of radiological protection, including very clear laws and regulations, specialized personnel and their regulatory bodies, research institutions and all necessary technicians for evaluation devices [29], [31]. On the other hand, in underdeveloped African countries of which Mozambique is a part, and in Asian countries in general, infrastructure continues to be a challenge, as well as the integration of regulations and laws, qualified human resources and regulatory bodies, this due to the lower degree of economic difficulties and political instability. ECDC dose reduction is a reality in many practices due to the implementation of radiological protection optimization principles [28].

Current International Standards for Radiation Protection and Safety of Radiation Sources (BSS) supported in collaboration with different organizations such as the Food and Agriculture Organization of the United Nations (FAO), the IAEA, the International Labor Organization (ILO), the (ECDC) communities [9], the Pan American Health Organization (PAHO) and the World Health Organization (WHO) provide a set of appropriate recommendations and procedures for developing national radiological protection laws and regulations as well as operational requirements [7].

## 1.6. Current challenges and developments in radiation protection

Radiation protection is a dynamic area, and its definition is constantly changing. Despite new technological advances regarding protection from the use of radiation sources. However, practical and conceptual challenges and issues regarding radiological protection continue to arise daily [4].

Advances in cell biology have brought significant results in understanding the behavior of cancer cells in the presence of radiation. This advance allows us to verify dose-effect and risk models, as well as genetic analysis techniques that allow us to

identify some specific induced tumors [30], including their exact location. On the other hand, these advances at cellular levels can affect how radiation practices are carried out in all processes. Experimental data indicate that stimulation of cellular repair at very low doses can affect estimates of stochastic risk and lead to situations involving intervention [16].

In terms of sources used in medicine for diagnosis and treatment, industry, waste disposal and research there are lot of challenges that need to be addressed in the field of radiation protection. Injuries and deaths are frequently reported caused by accidents and errors in the use of ionizing radiation, as well as used equipment [29], [4]. These situations are more serious when it comes to high doses for treatments. This suggests the need to improve the techniques and use of ionizing radiation, including effective measures and the management of systems that can reduce errors and make treatment more precise [11].

Regarding waste disposal, we also find the main difficulties related to an adequate safety analysis and the lack of information to create models to predict risks. To mitigate these difficulties requires efforts from national and international organizations in the field of radiation protection [30].

## 1.7. Implementation of a Nuclear Medicine Service

Nuclear medicine is a specialty of medicine that uses radioactive isotopes for application in diagnostic and therapeutic in patients. Indeed, numerous diseases such as endocrinological, cardiological and neurological diseases use nuclear medicine, with emphasis on cancer diseases as more than 80% of all procedures used in nuclear medicine are based on cancer therapy [32].

Nuclear Medicine facilities for its implementation are important to consider 3 main requirements as space, equipment and staff. The size of Nuclear Medicine services is related to space requirements and according to the level of services provided whether in vitro or in vivo imaging laboratory [33]. There are 3 levels of nuclear medicine service as shown in table 1, to implement Nuclear Medicine facilities.

Table 1.1 Levels of nuclear medicine service.

| |
|---|
| **Level 1:** this level is required where gamma camera equipment is needed for imaging goals, with single room close to the reporting room where the staffs share their |

ideas and the radiopharmaceutical, radiation protection and physics are hired off-duty is recommended for private service [33].

**Leve 2:** adequate for hospitals where is needed a multiple imaging rooms in which non-imaging and in vitro studies will be taken place as well radionuclide treatment [33].

**Level 3:** necessary when an academic institution focuses on research for cancer treatment, as well as the continuous development of workers following structured programs, it also includes a room for inpatient and outpatient therapy [33].

In addition to the levels of nuclear medicine service presented previously, in the case of in vivo diagnostic procedures, the existence of a radiopharmaceutical to measure doses within the service as well as the 99mTc generator is essential [11]. The structure and plan in the initial phase must take into account different factors such as space for routine testing and staffing needs. The nuclear medicine service must also consider the issues of radiological protection when constructing the building [33], namely:

- It is recommended that the painting of laboratory walls and doors is of good quality;
- Worktables must be smooth and laminated;
- Floors must not allow the entry of water or any other liquid;
- Must have lead-shielded containers;
- Remote manipulation equipment must be available;
- Ventilation to clean dirt and dust.

Nuclear medicine must have competent workers capable of managing and interacting with Physicians, hospital and financial managers, it must also have a governmental partition, insurance companies [28]. Other recommendations in the implementation of nuclear medicine service include information to be shared with patients and the public about treatment, for better interaction with patients and cooperation during treatments [32].

To better design a nuclear medicine service, it must be preceded by study of the demographics of the population and the prevalence of diseases in the respective country [29]. This study is the basis, as it will allow us to know which levels of nuclear medicine service will be appropriate including the socioeconomic development of the country or region and size of the country, population and capacity to manage nuclear medicine training programs for the entire working class [34].

## 1.8. Components of the Nuclear Medicine service

A nuclear medicine service must consider the following list of aspects [33]: adequate level of service, equipment with appropriate specifications, qualified human resources, fire and building safety codes, must have a delivery policy that includes equipment testing, control manuals, service management, experience exchange programs between workers and research projects and future perspectives. It is important to highlight some points listed above, beginning with equipment used in nuclear medicine [33], [32] are: Dose calibrator, Gamma camera, SPECT, PET, PET/CT, SPECT/CT, stable power supply.

A nuclear medicine service, being a multidisciplinary field, needs collaborators from different collaborative teams and each of the collaborator teams has its own task as following in figure 1.15, which represents an overview of a management system in nuclear medicine service, highlighting the management, technical, administrative, primary and support processes. It should be noted that, each term in figure 1.15 is clearly explained:

1. Strategic planning: Involves strategic plans to guide the operations of the nuclear medicine service;
2. Customer relationship: Management of interactions with different classes such as patients, referring doctors and insurance companies;
3. Relationship with Scientific Societies: communication with relevant scientific societies;

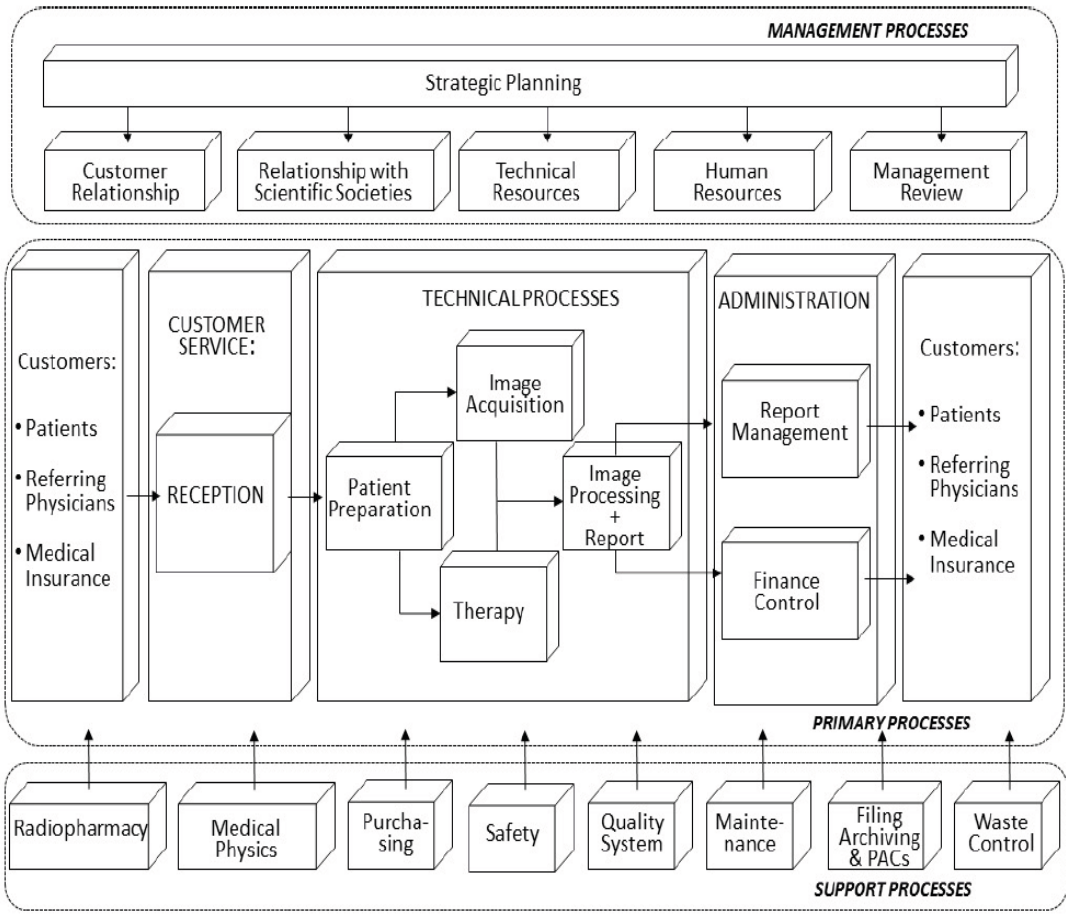


Figure 1.15. Management and support in Nuclear Medicine Service [34]

4. Strategic planning: Involves strategic plans to guide the operations of the nuclear medicine service;
5. Customer relationship: Management of interactions with different classes such as patients, referring doctors and insurance companies;
6. Relationship with Scientific Societies: communication with relevant scientific societies;
7. Technical Resources: Management of technicians necessary for service operations;
8. Human Resources: area responsible for the management and development of personnel working in the nuclear medicine service;
9. Management review: Evaluates service performance and implementation of continuous improvements;
10. Image acquisition: obtaining medical images using different nuclear medicine techniques;

11. Image processing and reporting: Analysis and interpretation of the images obtained, followed by the preparation of reports;
12. Therapy: Treatments carried out using nuclear medicine techniques;
13. Report management: Organization and management of all reports generated during technical processes;
14. Financial control: Financial management, including budgets, costs and payments;
15. Reception: First point of contact for patients, where initial care takes place;
16. Radiopharmacy: Production and management of radiopharmaceuticals used in procedures;
17. Medical physics: Application of physics principles to the safety and effectiveness of procedures;
18. Purchasing: Acquisition of equipment and materials necessary for operations;
19. Security: Implementation of security measures to protect patients and staff;
20. Quality system: Ensuring that all procedures meet quality standards;
21. Maintenance: Maintenance of equipment and facilities;
22. Archiving and PACS: Medical image archiving and communication system;
23. Waste control: Adequate management of waste generated, especially radioactive waste;
24. Patients: users of nuclear medicine services;
25. Referring Physicians: Physicians who refer patients to services;
26. Medical insurance: Entities responsible for paying for nuclear medicine services;
27. Patient Preparation: Prepare patients for imaging or therapy procedure.

## 1.9. International commission on Radiological Protection

The International Commission on Radiological Protection (ICRP) was founded in 1928 at the International Congress of Radiology with the International Society of Radiology. Its field of activity is radiological protection in medical exposure against ionizing radiation [29]. ICRP is a private organization located in the United Kingdom (UK) with support from different international and governmental organizations and is responsible for issuing recommendations linked to radiation protection principles, regulations, protocols [30].

ICRP first published its report in 1928, which consisted of recommendations implemented in September 1958. Then the general recommendations were issued in 1964 as Publication [35], then underwent changes as published [29] in 1966. These changes occurred until 1980 and 1987 when they were clarified and expanded by

succession of Declarations [36]. In 1991 the recommendations were definitively revised and issued resulting in Publication 60 [37]. Specialist-themed reports on ionizing radiation appeared later, resulting in subsequent publication numbers.

The primary objective of the Commission's recommendations is to provide an adequate standard of protection for humans without unduly limiting beneficial practices that give rise to radiation exposure [29]. The level of protection against ionizing radiation, rather than the best possible standard, regardless of costs and benefits, cannot be achieved based on scientific concepts, but also clinically proven. Some important publications are [38]:

1. Recommendations of the International Commission on Radiological Protection: Risks associated with ionizing radiation-1990 [38];
2. Annual limits on radionuclide intake by workers based on 1990 recommendations
3. Radiation protection 162 titled Criteria for Acceptability of Medical Radiological Equipment used in Diagnostic Radiology, Nuclear medicine and Radiotherapy [39].

Among other important publications. The recommendations of this commission are more used in the European Union when compared to other organizations of the same nature. In subsequent chapters we will return to the discussion on this ICRP subject.

# CHAPTER II

This chapter presents IAEA quality assurance in nuclear medicine, improvement and role of quality assurance, internal and external audits, limitation of checklists, coverage for clinical audits, guide to audit checklists and its limitations, as well preparation for QUANUM audits.

## 2. IAEA Quality Assurance in Nuclear Medicine

According to the IAEA, implementation of a quality Assurance in Nuclear Medicine involves different aspects to take into consideration and one of them is leadership and management, and should be structured as follows [33]:

- Managers should demonstrate leadership and commitment to quality and safety;
- NMS senior management must be responsible for establishing, applying, sustaining and continually operationally improving a Quality Management System (QMS) and must establish goals, plans and objectives consistent with the QMS and formulate them in a quality manual;
- Adequate interactions with all stakeholders (such as administrators, referring physicians, patient advocates) must be ensured and also QMS must integrate safety, environmental safety, quality, human and organizational factors;
- The QMS must be properly documented and each component readily available at the appropriate point of use;
- Managers must determine competencies and provide resources to carry out planned activities;

Adopting a QMS should be a strategic decision for an NMS. Various demands and restrictions, objectives, the nature of services supplied, the processes used, and the NMS's size and structure all have an impact on the design and execution. An NMS should develop, document, and maintain a context-appropriate QMS that is constantly enhanced in compliance with the needs of professional, regulatory, accrediting, or standards authorities [12]. A QMS seeks to help the NMS meet the standards outlined in its quality policy while also satisfying its customers [34]. The document must have:

- Contains all license details;
- A quality handbook that should clearly define purpose, vision, strategy, quality policies, and objectives, as well as a description of the organization and its structure.

- Standard operating procedures for primary diagnostic and therapy management and support processes, as indicated in the process map, in written form hard copy or electronic.
- External/reference documents such as indicators and parameters, Non-conformances and preventive/corrective actions

Another aspect to bear in mind is the audit team in nuclear medicine service, considered as an indispensable part of quality management. In summary, the audit team plays a vital role in ensuring the quality, safety, and regulatory compliance of nuclear medicine service [25]. Their independent evaluation, compliance monitoring, risk identification, and quality improvement efforts are essential for maintaining high standards of care and continuous enhancement of services [31].

## 2.1. Improvement and the role of quality assurance in Nuclear Medicine

The objective of quality assurance is to review and evaluate through observation and collection of evidence on the practices of an NMS, with a special focus on service quality aspects, in accordance with the QUANUM criteria [10]. This includes elements involved in the different processes, such as commitment to quality, optimal patient care, best practice standards for imaging and radionuclide therapy, adequacy of facilities and personnel, and professional competence [16].

In general, clinical audits should be multidisciplinary, encompassing all experts involved in providing the service. However, in specific instances, a single discipline audit may be appropriate [29]. It should also include information about equipment and processes, as well as the protection and safety of patients, workers, the public, and the environment. The NMS's overall performance, as well as its interactions with other departments within the institution and with external services and providers, should be evaluated [34].

Before beginning the audit, the final makeup of the audit team should be informed to the NMS staff [9]. A comparable team may be necessary to follow up on the audit's findings and recommendations. The IAEA suggests using this instrument for self-assessments to improve clinical practice and identify areas for improvement [12].

Clinical audits should be carried out on a regular basis, and the audit cycle should be finished by closing the loop and implementing the proposed modifications. The audit cycle involves selecting a good practice standard, comparing it to local practices, making required changes, and re-auditing after a set period of time [8]. A significant aspect of

the audit cycle is that clinical audits typically result in the adoption of change that improves practice and, eventually, benefits patients. Regular re-audits increase quality and provide confidence that it is maintained. Re-audits are necessary to verify that progress is maintained [12].

Conducting audits on a regular basis allows an NMS to continuously improve the quality and safety of its services. The sequence of steps followed in this process are shown in figure 2.1.

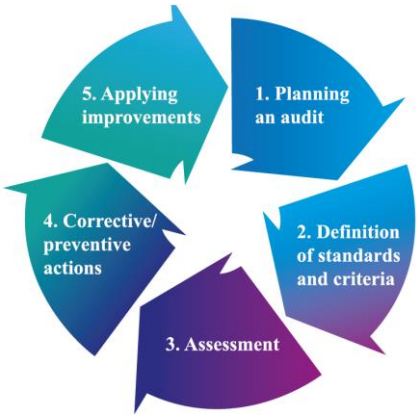


Figure 2.1. The concept of the cycle of continuous improvement [32].

The quality management program is critical for providing improved patient care and is an essential tool in today's healthcare system. It also offers an objective instrument for prioritizing and justifying the utilization of limited resources. All safety-related issues should be addressed and prioritized [28]. Implementing a timetable for internal and external audits should be included in the NMS calendar. Internal audits could be conducted over a period of several months, with a few checklists completed each month. A busy clinical environment should not be an excuse to skip the audit procedure [29]. Audits can be divided into two groups nominated Internal Audits and External Audits as will see soon. An audit team consist of the following members:

- Nuclear Medicine Physician;
- Medical Physicist;
- Radiopharmacist;
- Nuclear Medicine Technologist;
- Nurse;
- Administrative Staff Member;
- Representative of the institutional quality department.

## 2.2. Internal Audits

Internal audits are scheduled reviews on essential components of the NMS to determine whether it is providing high-quality healthcare services with low risk. Staff members can be taught and qualified as quality system evaluators to conduct regular audits of the quality system's operations [34]. Internal audits can also be carried out by other hospital employees or through a peer review by professionals from other institutions. Internal audits activities involve:

- Nuclear Medicine Services should have an internal audit performed on an annual basis;
- An audit could be limited to a subset of the processes involved in providing clinical services;
- An internal audit team should be constituted, usually consisting of representative staff members from various specialties;
- Assessments should rely on seen evidence, such as written documentation, Service Operation Procedure, on-site photos, and staff interviews;
- The audit checklists in QUANUM publication help internal and external auditors evaluate service performance against best practice standards;
- Identify potential risks, shortcomings, or non-conformances and develop action plans accordingly;
- Action plans should prioritize preventative or corrective activities, assign them to appropriate individuals, and implement them on time. If chances for improvement are found, appropriate measures can be addressed and established as NMS quality objectives;
- Routine activities begin after standards are satisfied or preventive/corrective actions are successfully executed.

## 2.3. External Audits

The external audit is generally carried out by a committee of professionals certified by the competent and independent body, such as the IAEA or an association scientifically recognized for its competences, such as a regional or national nuclear medicine association [34]. The most important aspect to take into consideration in this process is that the external audit must be understandable and practical.

A more practical option often adopted is to carry out partial internal audits, or sector-by-sector audits, according to a program that results in the spreading of a complete audit over a period of one or even two years [25]. External audit can be applied when:

- Compliance with the requirements and criteria stated by the National Safety and Quality Health Service criteria;
- Provision of high-quality imaging and therapeutic treatments in a secure environment;
- Referral triage, with prompt scheduling and appointment allocation;
- Radiation management under safety criteria specified by regulatory agencies such as the IAEA, the European Association of Nuclear Medicine (EANM), or the Society of Nuclear Medicine and Molecular Imaging (SNMMI);
- Identifying patients in conformity with national and international norms;
- The appropriateness or clinical rationale of diagnostic or therapeutic treatments and compliance with hospital infection control polices.

## 2.4. Coverage for clinical audits

Clinical audits should follow a road map defining a patient's course of care. Clinical practices are combined to provide effective, resource-efficient, and appropriate therapy for a given ailment, procedure, or symptom [11]. Audits should encompass all stages of the clinical process to improve overall care quality. Clinical audits should focus on three key aspects of healthcare practices:

- ***Structure:*** refers to the characteristics of the places in which care occurs. This encompasses the characteristics of material resources (such as facilities, equipment, and money), human resources (such as personnel numbers and qualifications), and organizational structure (such as staff organization and reimbursement systems).
- ***Process:*** refers actual act of providing and receiving care. It covers both the patient's activities in seeking and receiving care, as well as the practitioner's activities in diagnosing and proposing or executing therapy.
- ***Outcome:*** refers to how care affects the health of individuals and populations. A comprehensive definition of health status includes improvements in the patient's knowledge as well as salutary changes in the patient's behavior.

Clinical audits often evaluate structure and process, while evidence-based medical research assesses practice outcomes. This is especially true for external audits, when it is difficult to implement the requisite long-term outcome assessment, unlike internal audits. External audits often analyze solely the quality of follow-up procedures [10].

## 2.5. Guide to audit checklists and their limitation

The International Atomic Energy Agency developed a comprehensive program known as QUANUM-Quality Management Audits in Nuclear Medicine [4]. One of intended program is checklists but is not exhaustive tool for quality assessment. Because an audit is an observation made at a certain point in time, the evidence obtained may be limited. Users are urged to consult current IAEA publications and scholarly literature, as well as nuclear medicine professional society guidelines. It should be highlighted that expert judgment is always necessary for a thorough evaluation. Additionally, audit checklists are not designed for the following:

- ***Regulatory purposes:*** Audit teams provide objective advice on quality improvement rather than enforcing it. ***Accident investigations***: are not conducted by audit teams. In such circumstances, a more targeted and department-specific technical study is necessary.
- ***Research:*** study: The purpose of this program is neither to assess the quality and safety of any form of study, nor to determine whether institutes are eligible to participate in joint clinical trials. Peers involved in the study conduct these assessments, which will focus on an institute's tight adherence to a specific, stated clinical protocol for a chosen set of patients, as well as accompanying quality control***.***
- ***Interdepartmental comparison***: This program is not intended to be used for interdepartmental comparison.
- ***Training programs***: This program is not intended to be used for evaluation of the quality of training programs in which an NMS may be involved.

All information collected during the audit is compiled in a questionnaire made up of fourteen checklists based on Excel spreadsheets, covering all aspects of the audit. The questionnaire begins with management and quality system checklists, and then addresses issues of radiation safety, equipment QA, clinical services and radiopharmacy. Using drops down menus, and a scoring mechanism, all applicable items are scored according to their level of compliance. The auditor must complete notes and comments justifying the score. The spreadsheet tool includes:

- A color code for quickly viewing compliance status;
- Examples of results and evidence to be collected and links to reference documents for each item;

- Spaces for comments and planned actions, with proposed dates;
- A summary at the top of each checklist, reporting the results and number of non-conformities;
- Items marked as 'not applicable' are not used in evaluating the final score.

The International Atomic Energy Agency (IAEA) has developed the QUANUM (Quality Audits of Management in Nuclear Medicine) program, which covers all aspects of nuclear medical practices, including clinical practice, management, operations and services. The program includes detailed quality standards in checklists, aiming to introduce a culture of comprehensive, patient-oriented, systematic, and results-based quality audits.

## 2.6. Preparation for the QUANUM Audits

An audit's success is dependent on all parties involved being thoroughly prepared. The audit schedule should be agreed upon by the team and the person in charge of the NMS. The audit team should have quick access to all relevant documentation from past audits [4]. The audited Nuclear Medicine Services role is to:

- Prepare all necessary documentation in advance;
- Provide previous audit reports;
- Inform all hospital workers about the audit schedule;
- Identify and include team members;
- Guarantee the independence of auditors and collaborate with them;;
- Provide the necessary resources for auditing. For external audit: prepare a presentation in advance about the NMS..

## 2.7. Relevant IAEA documents on Quality Assurance in Nuclear Medicine

The International Atomic Energy Agency (IAEA) gives relevant documents on quality assurance in nuclear medicine. These documents provide comprehensive guidelines, recommendations and protocols for good practices in nuclear medicine. The most important IAEA documents and their contents are highlighted below.

### I. Quality Management Audits in Nuclear Medicine Practices (QUANUM)

This document summarizes the QUANUM audit program, which stresses improvement of quality assurance in nuclear medicine facilities through systematic.

QUANUM includes guidelines and fourteen check lists emphasizing how to conduct audits, basic standards to be followed and the procedures of implementing improvements based on audit findings.

### II. Quality Assurance for SPECT Systems

This document gives detailed guidelines for Single Photon Emission Computed Tomography (SPECT) systems. It covers all basic procedures ensuring that all requirements are met the condition of accuracy and readability of SPECT for good practices, maintenance procedures and performance evaluations to ensure the best results in diagnostic.

### III. Quality Assurance for PET and PET/CT Systems

This publication provides guidelines for Positron Emission Tomography (PET) and PET/CT systems. It stresses quality control mechanisms, calibration processes and routine checks in order to maintain the performance and safety of their imaging systems.

### IV. Quality control in Nuclear Medicine

This document gives a comprehensive framework for quality control for good practices in Nuclear Medicine. It covers protocols for equipment testing, patient safety and training requirements for staff to maintain better standards in nuclear medicines services.

### V. Nuclear Medicine Resources Manual

This publication addresses resources for setting up and how to manage nuclear medicine facilities. It is designed for equipment specifications, radiation safety and clinical guidelines and approach to quality assurance in nuclear medicine.

All these documents provide high quality procedures in nuclear medicine service ensuring highest standards of safety, accuracy and effectiveness, protecting workers and patients.

# CHAPTER III

This chapter discusses the quality assurance of nuclear medicine by the European Commission, emphasizing the General Principles of Radiological Protection in Nuclear Medicine, Dose Restrictions for Occupational, Public and Medical Exposure, Reference Levels in Nuclear Medicine, Dose Limits for Occupational Exposure and Volume Dosimetry in Nuclear Medicine.

## 3. European Commission Quality Assurance in Nuclear Medicine

Council Directive 2013/59/Euratom of 5 December 2013 [3], establishes basic safety standards to protect against dangers arising from exposure to ionizing radiation. This directive repeals Directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom [40] and 2003/122/Euratom. The main points of the directive include:

- Justification of Medical Exposure: Reinforces the need for justification for medical exposures, including in asymptomatic individuals.
- Patient Information: Introduces requirements to inform patients about exposures.
- Recording and Reporting Doses: Strengthens the requirements for recording and reporting doses from radiological procedures.
- Diagnostic Reference Levels: Requires the use and regular review of diagnostic reference levels, including for interventional procedures.
- Dose Indicators: Promotes the availability of dose indicator devices.
- Medical Physics Specialists: Highlights the role and support of Medical Physics Specialists in imaging.
- New Definitions and Dose Limits: Introduces new definitions and establishes a new dose limit for the lens.
- Procedures in Asymptomatic Individuals: Regulates image exposures and procedures in these individuals.
- Transfer of Dosimetry Information: Requires the transfer of this information to exam reports.
- Responsibilities and Records: Defines new requirements on responsibilities and the recording and analysis of accidental or unintentional exposures.
- Population Dose Assessment: Requires assessment based on distribution by age and sex.

These points will require adaptations to regulations, practices, and equipment to maintain high standards of radiation safety. The basic safety criteria in this regulation include new recommendations from the International Commission on Radiological Protection (ICRP) and have been updated to reflect new scientific data and operational experience. The European Union Council unanimously approved the directive [3], following four years of effort by multiple European scientific and technical bodies. According to the press release issued following the Council meeting in Brussels, the new directive requires Member States to establish legal requirements as well as an appropriate regulatory control regime that reflect a radiation protection system based on the principles of justification, optimization, and dose limitation for all exposure situations.

The directive requires an elevated level of expertise and a clear description of obligations among medical exposure experts to provide sufficient patient protection during radiodiagnostic and radiotherapeutic operations. This includes physicians, dentists, and other health care professionals who are clinically responsible for individual medical exposures, as well as medical physics specialists and other professionals who perform hands on medical radiology procedures, such as radiologists and technicians in radiodiagnostic medicine, nuclear medicine, and radiation therapy.

## 3.1. General principles of radiation protection in nuclear medicine

The primary concepts of radiation safety in nuclear medicine strive to reduce ionizing radiation exposure for patients, healthcare professionals, and the public while maintaining diagnostic and therapeutic benefits. These principles are influenced by international standards and recommendations, notably those from the International Commission on Radiological Protection (ICRP) [29].

Article 5 of the Council Directive 2013/59/Euratom of 5 December 2013 establishes that the Member States shall establish legal requirements and an appropriate regime of regulatory control which, for all exposure situations, reflect a system of radiation protection based on the principles of justification, optimization, and dose limitation:

The Council of the EU is the institution representing the member states' governments. Also informally known as them EU Council, it is where national ministers from each EU country meet to adopt laws and coordinate policies.

a) **Justification:** decisions introducing a practice shall be justified in the sense that such decisions shall be taken with the intent to ensure that the individual or societal benefit resulting from the practice outweighs the health detriment that it may cause. Decisions introducing or altering an exposure pathway for existing and emergency exposure situations shall be justified in the sense that they should do more good than harm.
b) **Optimization**: radiation protection of individuals subject to public or occupational exposure shall be optimized with the aim of keeping the magnitude of individual doses, the likelihood of exposure and the number of individuals exposed as low as reasonably achievable taking into account the current state of technical knowledge and economic and societal factors. The optimization of the protection of individuals subject to medical exposure shall apply to the magnitude of individual doses and be consistent with the medical purpose of the exposure, as described in Article 56. This principle shall be applied not only in terms of effective dose but also, where appropriate, in terms of equivalent doses, as a precautionary measure to allow for uncertainties as to health detriment below the threshold for tissue reactions.
c) **Dose limitation**: in planned exposure situations, the sum of doses to an individual shall not exceed the dose limits laid down for occupational exposure or public exposure. Dose limits shall not apply to medical exposures.

## 3.2. Dose constraints for occupational, public, and medical exposure

The Directive in their article 6, following the ICRP guidance establish that the Member States shall ensure that, where appropriate, dose constraints are established for the purpose of prospective optimization of protection [3]:

a) For occupational exposure, the dose constraint shall be established as an operational tool for optimization by the undertaking under the general supervision of the competent authority. In the case of outside workers, the dose constraint shall be established in cooperation between the employer and the undertaking.
b) For public exposure, the dose constraint shall be set for the individual dose that members of the public receive from the planned operation of a specified radiation source. The competent authority shall ensure that the constraints are consistent with the dose limit for the sum of doses to the same individual from all authorized practices.

c) For medical exposure, dose constraints shall apply only with regard to the protection of carers and comforters and volunteers participating in medical or biomedical research.

Dose constraints shall be established in terms of individual effective or equivalent doses over a defined appropriate time period.

## 3.3. Reference levels in nuclear medicine

In nuclear medicine, reference levels are expressed as a function of administered activity. The amount of administered activity depends on the size and weight of the patient, and these characteristics influence both the distribution of the radiopharmaceutical throughout the body and the amount of tissue that the emitted photons must cross before reaching the detector [26].

Therefore, the reference levels are defined for a standard group of patients with similar weights. When it comes to pediatric patients, establishing reference levels is more challenging, as there is a wide range of patient sizes and therefore cannot be considered a standard patient. Thus, there is a need to adjust the activity administered taking into account their weight [41].

These adjustments are made using the European Association of Nuclear Medicine (EANM) Dosage Card. The equipment will also influence the establishment of the reference levels, since the sensitivity of the detector and the characteristics of the equipment can significantly interfere with the quality of the image obtained, influencing the amount of administered activity necessary to obtain a quality image.

Article 7, reference level from Directive 2013/59/Euratom [3] of 5 December 2013 refers that:

a) Member States shall ensure that reference levels are established for emergency and existing exposure situations. Optimization of protection shall give priority to exposures above the reference level and shall continue to be implemented below the reference level.

b) The values chosen for reference levels shall depend upon the type of exposure situation. The choices of reference levels shall take into account both radiological protection requirements and societal criteria. For public exposure the establishment of reference levels shall take into account the range of reference levels.

c) For existing exposure situations involving exposure to radon, the reference levels shall be set in terms of radon activity concentration in air as specified in Article 74 for members of the public and Article 54 for workers.

## 3.4. Dose limits for occupational exposure

Scientific information on tissue reactions requires better protection of the lens and following ICRP guidelines, the Directive 2013/59/Euratom of 5 December 2013 considers the occupational dose limit for the ocular lens to 20 mSv/year relatively. It should be noted that this value is relatively low when compared to the Directive's previous value of 150 mSv/year [3].

This Articles 9 on dose limits for occupational exposure indicate that:

1. Member States shall ensure that dose limits for occupational exposure apply to the sum of annual occupational exposures of a worker from all authorized practices.
2. The limit on the effective dose for occupational exposure shall be 20 mSv in any single year. However, in special circumstances or for certain exposure situations specified in national legislation, a higher effective dose of up to 50 mSv may be authorized by the competent authority in a single year, provided that the average annual dose over any 5 consecutive years, including the years for which the limit has been exceeded, does not exceed 20 mSv.
3. In addition to the limits on effective dose laid down in paragraph 2, the following limits on equivalent dose shall apply:
    a) The limit on the equivalent dose for the lens of the eye shall be 20 mSv in a single year or 100 mSv in any five consecutive years subject to a maximum dose of 50 mSv in a single year, as specified in national legislation.
    b) The limit on the equivalent dose for the skin shall be 500 mSv in a year, this limit shall apply to the dose averaged over any area of 1 cm, regardless of the area exposed;
    c) The limit on the equivalent dose for the extremities shall be 500 mSv in a year.

## 3.5. Clinical Dosimetry in Nuclear Medicine

The European commission in its Directive 2013/59/Euratom in its article 56 referring to the target volume of ionizing radiation exposure in nuclear medicine for treatment

purposes, states that there must be an individualized treatment plan with carefully verified dose delivery. In the same article, the Directive extends to the involvement of Medical Physics Expert in all stages of treatment [5].

The European Association of Nuclear Medicine (EANM) has categorized three levels according to the directive's optimization principle, based on prescription, recording and notification of absorbed doses. In recent times, a greater number of treatments based on nuclear medicine in Europe have been standardized [32]. The three levels are:

I. **Level 1:** prescription based on patient activities and average dosimetry. Administration of the activity is 10% of the intended activity, according to EANM guidelines. The difference between activity measured and administrated corresponds to net activity [33]. Thus, is important to make sure that the dose calibrator for measuring the radionuclide is calibrated. The absorbed dose can be calculated for patients whose treatment falls into level 1 using patient average dosimetry data and administered activity. To this end, there must be sufficient information for the physician to make a correct decision about the effectiveness of treatment at level 1, knowing in advance that the absorbed dose for the target volume is not available at level 1.
II. **Level 2:** to achieve this level, it is important to record and report the dose absorbed in the organs at risk, this will result in compliance, being the most recommended level for non-standard therapies. In treatments, the combined standard uncertainty in absorbed dose is within 20%, depending on treatment goals. This level is more suitable for children since optimization of the absorbed dose is essential [32].
III. **Level 3:** for this level 3, it is essential that the dosimetry and the correlations between the absorbed dose and the induced effects are identified, this can allow us to better understand the characteristics of the tumor as well as complication profiles of normal tissues, resulting in more precise dose-effect reduction. Level 3 fits into personalized treatment and any uncertainty in absorbed doses must be communicated immediately. In general, this level provides complete information on the absorbed dose assessment steps, which allows reproducibility and expansion of results [32].

## 3.6. Relevant European Commission documents in Nuclear Medicine

The European Commission (EC) has published many important documents addressed to quality assurance in nuclear medicine giving guidelines and protocols to ensure safe and effective procedures of their management in the European community.

**I. Radiation protection 91 titled Criteria for Acceptability of Radiological in Radiotherapy and Nuclear Medicine Installations**

This publication stresses criteria for the Acceptability of Radiological in Radiotherapy and Nuclear Medicine Installations. It provides guidelines and recommendations on equipment performance, quality control, radiation safety and staff qualifications for nuclear medicine facilities in order to meet desirable standards of safety and effectiveness.

**II. Radiation protection 162 titled Criteria for Acceptability of Medical Radiological Equipment used in Diagnostic Radiology, Nuclear medicine and Radiotherapy**

This document gives criteria for the Acceptability of medical radiological device addressing diagnostic Radiology, Radiotherapy and Nuclear medicine. It covers technical aspects, performance testing, radiation protection measures and maintenance requirements for good practices of the use of radiation and radioactive materials.

**III. Radiation Protection 159 titled European commission guidelines on clinical audit for medical radiological practices (diagnostic radiology, nuclear medicine and radiotherapy)**

Provides guidelines for Computed Tomography (CT) and extends to PET/CT and SPECT/CT modalities. It includes quality criteria for image quality, dose optimization, patient safety and quality control applicable to nuclear medicine practices including CT imaging.

**IV. Radiation Protection 175 designed Guidelines on Radiation Protection Education and Training of Medical Professionals in the European Union**

This guideline stresses the importance of education and training of staff in radiation protection for medical exposure in nuclear medicine. Gives idea for training programs, curriculum specifications and competency needed to ensure that workers are trained in radiation protection procedures for good practice in nuclear medicine.

## V. Radiation Protection 180 known as Medical Radiation Exposure of the European Population

This publication provides an overview of the use of radiation in medicine in the European Community including data on nuclear medicine procedures. It covers different topics such as dose distribution and impact of different medical practices on radiation exposure addressing quality assurance and optimization in nuclear medicine services.

## VI. Radiation Protection nº 174: European guidelines on medical Physics Expert

This report provides a framework of European guidelines for specialists in medical physics. Includes curriculum and requirements for Medical Physics Expert certification.

These documents highlighted above gives comprehensive framework for quality assurance program in nuclear medicine in particular equipment standards, recommendations and protocols to be followed, training program for workers and patients care. Many of the Directives in the European Community are made up of these collective documents.

# CHAPTER IV

In this chapter, we analyze a comparative of the IAEA and EC recommendations on quality assurance in Nuclear Medicine, the current situation of Medical Physics in Mozambique.

## 4. Comparative Analysis of IAEA and EC Recommendation

The International Agency Energy Atomic (IAEA) and the European Commission (EC) are known as the biggest organizations in the world, leading especially guidelines for the use of ionizing radiation in different areas of human activities. Therefore, both IAE and EC provide guidelines and recommendations for good practices of radiation and radioactive substances, this is the common point between both. Despite this convergence, they differ in two main moments namely in scope and implementation models. Below is highlighted a comparative analysis of their recommendations between IAEA and EC:

- The IAEA supply international standards and guidelines for the use and management of radioactive substances and radiation in its member states in the world;
- Provide a huge topic such as nuclear safety, security, safeguards and radiation protection in industry and medial exposure;
- The main goal is promoting safe, secure and good practices of nuclear technology in the world.
- The IAEA´s recommendations are applicable globally and supply a framework that member states can follow and adapt to their specific national regulations;
- The IAEA’s recommendations stress a risk-informed approach and good practices for implementation;
- The implementation of IAEA´s recommendations and guidelines is not mandatory;
- Provide programs and training for its member states;
- Supervisor missions to assist member states improving their nuclear safety and its security;
- Provide basic safety requirements for the protection of public and environment sated in General Safety Requirements (GRS);
- Continuous improvement, safety culture, approach based on risk and guidance and recommendations on fulfilling the Safety Guide (SG).

The IAEA´s recommendations and guidelines address frameworks adaptable to different region or national context in order to emphasis on international cooperation and support. European commission scope and recommendations:

- The scope of the EC includes Directives and regulations according to to EU law;
- The European Commission recommendations are directed at European Community;
- Emphasis on harmonizing radiation protection and nuclear safety standard across Europe to guarantee high levels of safety and environment protection;
- The supply very detailed and specific requirements, with quantitative limits and mandatory according to criteria;
- Provides Directives such as Council Directive 2013/59/EURATOM of 5 December 2013 laying down basic safety standards for protection against the dangers arising from exposure to ionizing radiation;
- Provides specific guideline on dose limits, exposure control and mandatory reporting mechanisms;
- The European Commission Directives must be transposed into local legislation by EU member states;
- Council Directive 2009/71/Euratom which establishes a community framework for the nuclear facilities;
- Recommends the high safety, radiation protection for public and workers and environmental protection;
- Assist and monitor compliance regarding assessments, inspections and violation of procedures if member states fail to comply with directives;

In general, European Commission’s recommendations is mandatory and must be applicable with specific legal requirements that must implemented by European Union member states, ensuring that all relevant issues are addressed with high degree of uniformity and enforceability within the EU.

## 4.1. Translation of IAEA and EU Recommendations for Mozambique

As Mozambique is an underdeveloped country, translating the IAEA and EU recommendations will require very in-depth work in all dimensions, from infrastructure to human resources with an internationally acceptable profile in nuclear medicine. Thus, it is important to provide the key documents and guidelines. In the meantime, are summarized critical documents and recommendations and their practical implications:

### I. Safety Standards Series Nº SSG-46 Radiation Protection and Safety in Medical uses of Ionizing Radiation (IAEA)

This publication contains comprehensive guidelines on radiation protection and safety for medical exposure and it includes frameworks, basic safety procedures, protection of patients and operational protocols. In this case, implication for Mozambique it requires to establish national regulation frameworks implementing safety procedures and guidelines in nuclear medicine facilities also continuous training human resources in radiation protection subject.

### II. Human Health Series Nº 33 titled Quality Assurance for PET and PET/CT (IAEA)

Provides topics focuses on the Quality Assurance procedures in nuclear medicine for PET and PET/CT systems, calibration procedures, performance testing and maintenance. Mozambique needs to implement Quality Assurance/Quality Control programs in nuclear medicine services addressing the accuracy of Diagnostic imaging and maintenance device standards.

### III. Safety Reports Series Nº 6 titled Quality Assurance for SPECT Systems (IAEA)

Discusses the Quality Assurance protocols for Single Photon Emission Computed Tomography (SPECT) systems. It stresses equipment performance, routine tests and image quality in nuclear medicine. Once again, implementation of QA/AC protocols in Mozambique will allow to maintain a good practices in Nuclear Medicine services improving Diagnostic accuracy and patient safety.

### IV. Safety Reports Series Nº 40: Applying Radiation Safety Standards in Nuclear Medicine (IAEA)

Outlines the application of Basic Safety Standards for radiation protection in nuclear medicine addressing guidelines for handling radioactive substances, patient dosimetry and occupational safety. Mozambique needs to establish radiation protection subject in Department of Nuclear Medicine in order to protect workers, patients according to international safety standards.

### V. IAEA: Quality Management Audits in Nuclear Medicine Practices (QUANUM)

This document summarizes the QUANUM audit program, which stresses improvement of quality assurance in nuclear medicine facilities through systematic. QUANUM includes guidelines and fourteen check lists emphasizing how to conduct audits, basic standards to be followed and the procedures of implementing improvements based on audit findings. It is important to Mozambique adopt this Audits in Nuclear Medicine to improve more in quality assurance program.

### VII. Radiation protection 91 titled Criteria for Acceptability of Radiological in Radiotherapy and Nuclear Medicine Installations (EC)

This publication stresses criteria for the Acceptability of Radiological in Radiotherapy and Nuclear Medicine Installations. It provides guidelines and recommendations on equipment performance, quality control, radiation safety and staff qualifications for nuclear medicine facilities in order to meet desirable standards of safety and effectiveness.

### VIII. Radiation protection 162 titled Criteria for Acceptability of Medical Radiological Equipment used in Diagnostic Radiology, Nuclear medicine and Radiotherapy (EC)

This document gives criteria for the Acceptability of medical radiological device addressing diagnostic Radiology, Radiotherapy and Nuclear medicine. It covers technical aspects, performance testing, radiation protection measures and maintenance requirements for good practices of the use of radiation and radioactive materials.

### IX. Radiation Protection 159 titled European Guidelines on Quality Criteria for Computed Tomography (EC)

Provides guidelines for Computed Tomography (CT) and extends to PET/CT and SPECT/CT modalities. It includes quality criteria for image quality, dose optimization, patient safety and quality control applicable to nuclear medicine practices including CT imaging.

### X. Radiation Protection 175 designed Guidelines on Radiation Protection Education and Training of Medical Professionals in the European Union

This guideline stresses the importance of education and training of staff in radiation protection for medical exposure in nuclear medicine. Gives idea for training programs, curriculum specifications and competency needed to ensure that workers are trained in radiation protection procedures for good practice in nuclear medicine.

### XI. Radiation Protection 180 known as Medical Radiation Exposure of the European Population

This publication provides an overview of the use of radiation in medicine in the European Community including data on nuclear medicine procedures. It covers different topics such as dose distribution and impact of different medical practices on radiation exposure addressing quality assurance and optimization in nuclear medicine services.

## 4.2. Medical Physics and challenge in Africa

The situation of lack of qualified medical physicists in most African countries continues to be a major problem in recent years, while their intervention plays an important role in better ensuring quality, safety and radiation protection for patients and the environment. Several studies indicate that most of the medical physicists who work in Hospitals do not have qualifications and qualifications as well as adequate training to carry out all activities in accordance with international standards in the three areas of Medical Physics: Radiotherapy, Radiology and Nuclear Medicine, in most cases African countries, with a greater and notable lack in the last two areas [42]. This problem is a reality in Africa, caused by the economic and social situation. There are several other associated problems, namely:

- There is a lack of local training centers with suitable curricula throughout the study process.
- Clinical training in recognized training centers is low.
- Organizing of the training of Medical Physicists by IAEA teams;
- Little or no support is given to the training of medical physicists by individual governments.
- Difficulty accessing training documentation.
- Lack of recognized bodies governing medical physics and local laws on the use of ionizing radiation in hospitals in many African countries.

- Ignorance about the role of the medical physicist on the part of hospital managers and health ministries.
- Lack of dosimetry, dose assessment and radiation monitoring equipment.

## 4.3. Current situation in Medical Physics in Mozambique

There is a severe shortage of qualified Medical Physicists to meet the growing demand in the Mozambique´s Hospitals and Healthcare Centers and limits the ability to provide high-quality treatments to patients. Furthermore, limited financial resources are an obstacle to the acquisition of modern equipment and the maintenance of existing equipment [42]. The lack of adequate funding also negatively impacts the ability to offer ongoing training and specialization to professionals in the field. Another problem Inadequate maintenance of equipment can lead to frequent failures and reduce the effectiveness of treatments. The shortage of technicians specializing in the maintenance of medical equipment is also a significant problem [43].

### 4.3.1. Radiotherapy, Radiology and Nuclear Medicine in Mozambique

In Mozambique, the radiotherapy service located at the Hospital Central de Maputo (HCM) was established on March 28, 2019 [42]. This is a treatment through which radiation is used ionizing agents to destroy the tumor or prevent its cells from growing, treatment of different types of cancer and other diseases, being until then the first and only one in the country. Now HCM only has one linear accelerator as seen in table, and the other is damaged, the only public hospital in Mozambique with Radiotherapy Services [42]. Regarding radiology and nuclear medicine, there are still no qualified professionals to bring radiological protection to a successful conclusion [42], which is one of the biggest challenges in oncology field.

Table 4.1- Distribution of radiological medicine equipment in Africa in 2022 [42].

| Country | Radiotherapy | | Diagnostic Radiology | | | Nuclear Medicine | | |
|---|---|---|---|---|---|---|---|---|
| | Teletherapy (Linac, Co-60) | Brachytherapy (LDR, HDR) | CT | FL / IR | Mammo | SPECT | SPECT/CT | PET/CT |
| Algeria | 37 | 12 | >570 | 170 | 280 | 24 | 11 | 1 |
| Angola | 3 | 1 | - | - | - | - | - | - |
| Benin | 0 | 0 | 5 | - | 6 | 0 | 0 | 0 |
| Botswana | 1 | 2 | - | - | - | - | - | - |
| Burkina Faso | 0 | 0 | 10 | - | - | 1 | 0 | 0 |
| Cameroon | 1 | 0 | - | - | - | 1 | 0 | 0 |
| Congo Republic | 1 | 0 | >10 | 0 | >5 | 0 | 0 | 0 |
| Cote D'Ivoire | 2 | 0 | - | - | - | 0 | 1 | 0 |
| Egypt | 110 | 23 | 725 | 622 | 185 | 72 | 15 | 52 |
| Ethiopia | 1 | 1 | 91 | 27 | 28 | 1 | 0 | 0 |
| Gabon | 2 | 0 | 12 | 5 | 13 | 0 | 1 | 0 |
| Ghana | 4 | 3 | 48 | 35 | 42 | 1 | 0 | 0 |
| Kenya | 11 | 5 | - | - | - | 1 | 1 | 0 |
| Libya | 6 | 1 | - | - | - | 2 | 3 | 1 |
| Madagascar | 2 | 0 | - | - | - | - | - | - |
| Mali | 1 | 0 | - | - | - | 0 | 0 | 0 |
| Mauritania | 2 | 1 | 1 | - | 1 | 0 | 1 | 0 |
| Mauritius | 3 | 1 | - | - | - | - | - | - |
| Morocco | 42 | 10 | 360 | - | - | 12 | 11 | 11 |
| Mozambique | 1 | 0 | - | - | - | - | - | - |
| Namibia | 2 | 1 | - | - | - | - | - | - |
| Niger | 0 | 0 | 10 | 3 | 10 | 0 | 2 | 0 |
| Nigeria | 10 | 6 | 150 | 8 | 50 | 2 | 1 | 0 |
| Rwanda | 2 | 0 | - | - | - | - | - | - |
| Senegal | 3 | 0 | - | - | - | 1 | 0 | 0 |
| South Africa | 97 | 24 | - | - | - | - | - | - |
| Sudan | 8 | 2 | - | - | - | - | 5 | 0 |
| Tanzania | 5 | 2 | 21 | 400 | <21 | - | - | - |
| Tunisia | 23 | 4 | 191 | 66 | - | 11 | 4 | 4 |
| Uganda | 1 | 1 | 26 | 1 | 12 | 0 | 1 | 0 |
| Zambia | 3 | 2 | 2 | - | - | - | - | - |
| Zimbabwe | 7 | 3 | - | - | - | 1 | 0 | 0 |

*CT – Computed Tomography; FL – Fluoroscopy; IR – Interventional Radiology; SPECT – Single Photon Computed Tomography; PET – Positron Emission Tomography; N/A – No Data Available

### 4.3.2. Professional certifications in Medical Physics

Despite Decree nº 49/2018 [44], 21 August Radiological Protection and Safety Regulations, in Mozambican territory, in its article 45 on equipment quality assurance it states that:

1. License holders must establish a quality assurance program for medical exposures, with the participation of a Radiologist, Medical Physicist, Radiotechnologist, Radiopharmacists and Radiochemist.

In the same decree in article 38, paragraph i, it says that [44]:

i) It is a radiological procedure requested by a requesting physician with clinical information from the patient or is part of an approved disease screening program; quality, as well as acceptance and commissioning of medical radiology equipment, must be led or supervised by a medical physicist.

However, despite this decree providing for the functions of a Medical Physicist in Mozambican territory, there is a gap which is the lack of clarity in terms of the requirements and qualifications of a Medical Physicist.

### 4.3.3. Radiation Protection Decree in Mozambique

Decree nº. 49/2018, 21 August Radiological Protection and Safety Regulations in its Article 44, on Calibration and Dosimetry says that [44]:

1. License holders must ensure that:

a) All radioactive sources that give rise to medical exposure are calibrated in accordance with the techniques and methods of reference laboratories;
b) Calibrations are carried out at the time of commissioning of the source, and in the future at time intervals duly submitted for evaluation by the Regulatory Authority;
c) Calibrations of radiotherapy units are subject to independent verification prior to commissioning.

2. The calibration of sources and dosimeters used for patient dosimetry may be assigned to a national or international dosimetry calibration laboratory.

This article, although it addresses the calibration of equipment and dosimetry, however, still leaves many gaps regarding clear procedures, how such commissioning tests are carried out, what are the guidelines for carrying out these tasks.

# CHAPTER V

This chapter contains practical implementation of the development program, human resources for maintaining the nuclear medicine service and the equipment necessary for this purpose.

## 5. Practical implementation of the quality assurance program

Nuclear medicine units must respect the general characteristics of health care units as well as some special characteristics regarding their design, structure and operational management, dictated mainly by requirements specific to radiological protection and functionality.

A properly designed nuclear medicine unit must guarantee the radiological protection of patients, workers and members of the public, respecting national legislation and applicable international recommendations. It must also provide convenient access and a comfortable environment. The dimensions of the unit must be appropriate to the techniques to be practiced, the number of exams to be carried out and the expected flow of patients.

The appropriate management of a nuclear medicine unit must take into account the individual contributions of those responsible for its design and construction, planning and organization of work, as well as radiological protection and quality assurance.

### 5.1. Human Resources

As said before, nuclear medicine service is a multidisciplinary field, needs collaborators from different collaborative teams and each of the collaborator teams has its own task as following:

#### 5.1.1. Physicians

Physicians must comply with the internal regulations of the health unit and collaborate with their supervisors in all areas. He must also maintain a practice of technical improvement and continuous training in their area of work, to correspond to an ever-higher level of service quality [9]. The nuclear Physicians is responsible for clarifying any doubts or questions requested by the prescribing doctor and guiding the examination to obtain the greatest diagnostic gain with the minimum radiation, risk or discomfort for the patient. The Physicians must study the images and integrate them with previous information, including comparison with previous studies. The preparation of the report,

in accordance with the recommended standards, must be done within a time frame appropriate to safeguarding the patient's interests [11].

### 5.1.2. Medical Physicists

Quality control of equipment must be ensured by a Physicist. Whenever justified, these professionals should have roles in the Radiation Protection Sector. They must comply with internal regulations and collaborate with the person responsible for the Unit in accordance with their duties [7]. In this case, qualification for a Medical Physicists in the European community should follow the framework according to EFOMP:

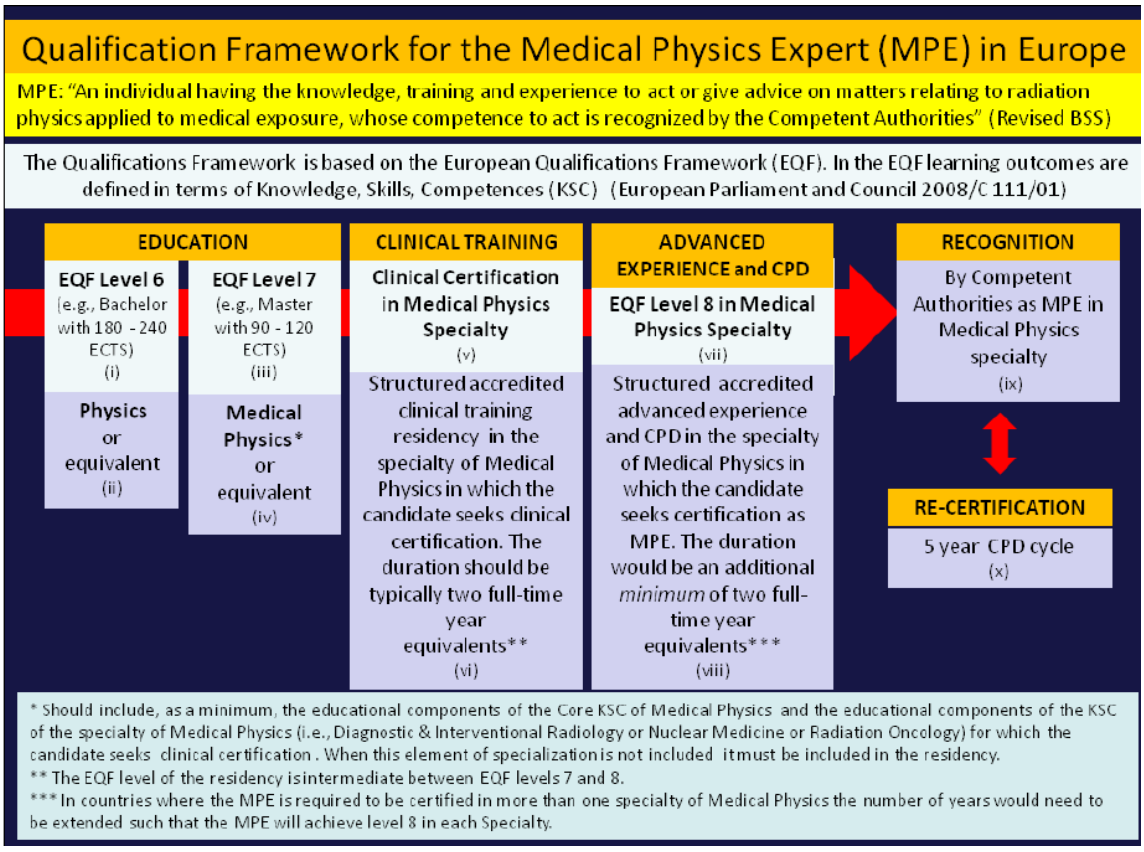


Figure 5.1. Qualification Framework for the Medical Physics Expert in Europe [45].

### 5.1.3. Radiopharmacists

Radiopharmacists are fundamental to the functioning of a nuclear medicine service, by ensuring the safe and effective use of radiopharmaceuticals for accurate diagnoses and effective treatments, ensuring that patients receive the best possible care.

### 5.1.4. Nuclear Medicine Technologist

There must be an adequate number of Nuclear Medicine technicians, duly qualified to carry out their functions and in accordance with international and national

legislation. Furthermore, they must comply with internal regulations and collaborate with the person responsible for the Unit in accordance with their duties. They must comply with and regulate their activities in accordance with the principles established in the Good Practices Manual.

### 5.1.5. Nursing, Administrative and Auxiliary Staff

Whenever it exists, it must be duly qualified to perform its functions. They must comply with the internal regulations and collaborate with the person responsible for the Unit in accordance with their functions and comply with and regulate their activities in accordance with the principles established in the Good Practices Manual.

## 5.2. Equipment

The basic equipment for operating a nuclear medicine service is presented below. In addition, characteristics, and tests of quality control to be carried out are also presented, as well as intervals and tolerance of equipment in accordance with acceptable national legislation and international standards. For better equipment performance, a quality assurance program discussed in previous chapters must be carried out.

### 5.2.1. Radiological Protection Equipment

Radiological protection is essential to ensure the lives of workers and the public against exposure to ionizing radiation in hospitals, radiology clinics and nuclear facilities. Radiation protection equipment monitors and reduces exposure to radiation. Personal Dosimeters are used to measure the accumulated dose of radiation received. In general, are instruments for measuring radioactivity assess contamination and Dose flow meters. This equipment must also be periodically calibrated.

Figure 5.2. Personal dosimeter [30]

### 5.2.2. Dose calibrator

Dose calibrators are used in clinical practices that involve the administration of a radiopharmaceutical for the detection and measurement of radioactive emissions [26], allowing the activity to be known before its administration to the patient. It is necessary

that these activity meters are capable of accurately measuring, in a wide range of activities and energies, the activity of a radionuclide, whether it is an emitter of γ or β rays [39]. The dose calibrator most used in the nuclear medicine service is composed of an electrometer, in a sealed ionization chamber [26], in a cylindrical shape with a central well where the radioactive source is positioned along the longitudinal axis z, and two electrodes with a difference of applied potential.


Figure 5.3. Shows the dose calibrator. IPO-Porto (not used actually)

Dose calibrator for doses to be administered must undergo periodic calibration and comply with the following main tests:

- ***Accuracy:*** is a test whose objective is to guarantee the traceability of the activity values determined by the calibrator to national or international standards within the indicated uncertainties [39]. This can be ensured by the secondary standard for all reference sources provided. The test, in practice, consists of one or more traceable standards positioned in a solid plastic matrix, in the shape of a bottle, with long-lasting radionuclides such as 133Ba (low energies), 57Co (intermediate energies) and 137Cs (high energies) recommended during acceptance testing [7]. Stability of the instrument must be checked for acceptance of the calibrator or after its repair and annually, with at least two traceable reference sources and the radionuclides must vary each year to include all commonly used radionuclides and fulfill all its energy range [17]. Radionuclides used during the daily accuracy test do not need to be repeated during this acceptance test. The suspension level is greater than 5% [39], according to national standards [45].

- ***Reproducibility:*** consists of a measure of the percentage deviation of at least ten consecutive measurements of the activity of a test source, the decay of which is negligible during the measurement period [26]. It is necessary to take care not to remove the support with the sample from inside the ionization chamber between measurements so as not to include possible errors associated with variations in the positioning of the source [32]. This parameter must be determined for each current range for which the calibrator is used, using sources with activities within the tested measurement range, and must be performed annually. The suspension level is greater than 5% [39], [45].
- ***Linearity:*** linearity test, defined as the ability of a dose calibrator to accurately measure the activity of a radioactive source over the range of values for which the specific radionuclide calibrator is used is determined by linearity testing [41]. This test records, at time intervals, the decay of a radioactive source with a high activity, normally higher than the activities used in a clinical environment, in order to verify whether the calibrator follows the expected decay curve for the source [6]. The current produced per unit of activity varies depending on the radionuclide used. Thus, the calibrator response is considered linear when the ratio between the measured and predicted response remains constant over the range of currents for which the calibrator was produced. Therefore, different radionuclides will have different activities where nonlinearities occur. The suspension level is greater than 1% [39].

### 5.2.3. Gamma Camera

Tests must be carried out upon receipt of the equipment, to check whether the operational parameters correspond to those indicated in the technical specifications provided by the manufacturer.

Figure 5.4. Illustration of Gamma Camera (dual head).

The standards of the National Electrical Manufacturers Association (NEMA) Standards Publication Nº. NU 1-2007 [14], Performance Measurement of Scintillation Cameras, must be respected. Periodic assessment of the camera's operating status, carried out through quality control tests, is essential to guarantee the quality of the results to be provided.

Each gamma camera must be evaluated in its acquisition capabilities in relation to the studies that are intended to be carried out and all the capabilities that are proposed by the manufacturer. Considering that gamma cameras have certain limitations regarding image uniformity, image linearity, spatial, intrinsic and extrinsic resolution, energy resolution and sensitivity, equipment over 10 years old must be tested in accordance with current recommendation [39]. The main routine tests recommended are:

- Intrinsic Spatial Resolution with the suspension level greater than 6mm;
- Intrinsic energy resolution with the suspension level greater than 15%;
- Multiple window spatial registration (for systems used for dual isotope studies) with 1 pixel the suspension level;
- Differential and Integral System/Intrinsic Non-uniformity with the suspension level greater than 7% [39], [46];
- Detector to detector Sensitivity variation (systems with opposing detectors) with the suspension level greater than 10%;

- System alignment (Systems with opposing detectors) with the suspension level greater than 1 pixel.

SPECT is a technique like gamma camera, in which gamma camera rotates around the patient's body and two-dimensional images are obtained at each projection angle, which, using appropriate mathematical image reconstruction algorithms, allow obtaining a three-dimensional image [10]. The more the detector number, the count number increases and consequently the spatial resolution increases resulting in the acquired image quality.

Figure 5.5. Dual-head SPECT/CT Camera at IPO-Porto [10]

The difference in relation to the equipment above is that it is hybrid, it performs SPECT/CT. A SPECT is a gamma camera, the acquisition mode changes in relation to the planar image. In addition to the parameters and criteria mentioned above, the following must also be considered:

- Field uniformity: camera uniformity must be controlled to ± 1%;
- Center of rotation: the deviation must be equal to or less than half an elementary surface cell (≤ 0.5 pixel) for a 128x128 matrix);
- Image and pixel dimension - the elongations in the X and Y directions must not differ by more than 5% [39] from each other;
- Alignment to the patient's bed: this alignment must be adjusted up to a limit of 2 mm after positioning the patient;
- Planar and transaxial spatial resolution must be determined for each equipment.

- Detector Movements: possible movements for the detector must be analyzed (rotation movement around an axis contained in the detector plane), longitudinal displacement of the detector, movement towards the patient's bed and the ability to rotate around the patient's bed, when applicable.
- Uniformity: Image uniformity is a critical measure of quality in medical imaging systems. Regular assessments and corrections ensure that the images obtained are of high quality and reliable for clinical use. Continuous in maintaining uniformity, it guarantees diagnostic and therapeutic accuracy. Lack of uniformity may indicate equipment problems, such as detector defects or calibration problems. There are two types of uniformity namely:
- ***Intrinsic uniformity****:* Intrinsic uniformity is determined from flood field images acquired without a collimator. To do that a 99m-Tc source is placed at approximately 5 times the uniformity field of view (UFOV) from the front face of the gamma camera. It is estimated that counting rate on the gamma camera is less than 30000 cps and the minimum counting for flood-field is about 4000 counts in each pixel of the image and then smoothed with a 9-point smoothing filter with the following weightings [5]:

| | | |
|---|---|---|
| 1 | 2 | 1 |
| 2 | 4 | 2 |
| 1 | 2 | 1 |

It is important to bear in mind that intrinsic uniformity must be considered Central Field Of View (CFOV) and Useful Field Of View (UFOV) and the measured values will meet or exceed the specification. Thus, uniformity intrinsic is divided into two groups: *integral uniformity and differential uniformity*.

***Integral uniformity*** is based on the maximum and minimum pixel counts in the image and is defined as:

$$IU = \frac{\max\_pixel\_count - \min\_pixel\_count}{\max\_pixel\_count + \min\_pixel\_count} \times 100\% \quad \text{Equation 5.1}$$

This relationship is valid for both cases CFOV as well as UFOV and the threshold values are typically 7% [46].

***Differential uniformity*** is defined as the change in counts of five consecutive pixels across all rows and columns of the image:

$$DU = \frac{\text{high} - \text{low}}{\text{high} + low} \times 100\% \qquad \text{Equation 5.2}$$

where “high” refers to the maximum count difference for any five consecutive pixels (row or column) in the image and “low” refers to the minimum count difference for any five consecutive pixels. This usually is reported for the UFOV.

- **Extrinsic uniformity** in which image acquisitions are made with a collimator. To ensure uniform irradiation, a narrow flood-field source of 99m-Tc or a disk source of 57-Co are mounted on top of the collimator. This protocol is more feasible for everyday quality assurance since the measurement can be performed without the collimator being removed. Extrinsic uniformity measurements offer the additional advantage of revealing any deficiencies or difficulties produced by the collimator itself [6].

### 5.2.4. Positron Emission Tomography (PET)

Positron emission tomography equipment, hereinafter referred to by the English nomenclature PET (Positron Emission Tomography), must be tested at the time of installation and before beginning clinical use. Subsequently, a quality control program must be established with two aspects: daily and annual.


Figure 5.6. Illustrates the PET/CT equipment at IPO-Porto.

This program must be designed and applied by a Medical Physicist Expert, that is, an individual competent in the independent practice of one or more areas of Medical Physics, with continuing education in the specific areas of work [5]. Daily quality control includes the following tests:

- Attenuation blanks;
- Operation of detectors;
- Normalization scans, if necessary.
- The “blank scan” is performed with cylindrical transmission sources and is used to monitor system stability and to determine which crystals, blocks and modules are more sensitive than the average of these system components. The following tests must be performed at least once a year:
- Spatial resolution (radial, tangential and axial);
- Count rate profile, including the correction factor: system dead time, count rate versus activity (scatter coincidences, random coincidences, background coincidences and true coincidences
- Sensitivity, uniformity, accuracy of attenuation correction calibration (quantification);
- Linearity of bed movement and reproducibility of the movement of transmission sources (extension and retraction);
- Reproducibility of the movement of lead septa extension and retraction;
- Image contrast and complete system testing (phantom study) and Instrumentation requirements

### 5.2.5. Computers

Computers coupled to gamma camera systems must meet the following requirements:

- Acquire data from one or more gamma cameras, analyze and visualize images related to this data and store them for later analysis and information collection;
- Be equipped with logical support that allows the functions set out in the previous paragraph to be carried out;
- The logical support in clinical terms must be analyzed depending on the tests that are intended to be carried out;
- Have peripherals and support means that allow you to archive each patient's data during the legally established period.

Figure 5.7. Computer for clinical purposes [10].

## 5.3. Quality Control Examples

Based on the proposed quality assurance program, several experiments and tests of equipment used in nuclear medicine services were carried out in accordance with the recommendations of the European Commission as well as the International Atomic Energy Agency. These aim to certify whether the equipment is in fact working normally or not, in order to guarantee the protection of patients and workers against ionizing radiation. The tests carried out as well as the procedures and methodologies used for each test are presented below. In addition to the tests, image quantification software was also developed using the Python programming language and then validated with ImageJ. In this section, we present an analysis of different measurements related to equipment testing.

### 5.3.1. Dose Calibrator: Linearity testing

The evaluation of the capability of a dose calibrator in measuring radioisotope activities at various magnitudes is essential via linearity testing. This testing is a crucial feature of the everyday operations of a nuclear medicine department and has implications for patient exposure.

#### A. Materials and Methods

Before starting this study, the calibrator was used to make sure that the good quality of the tools by testing its precision, accuracy, source shape, and daily limits. The radioisotope 99mTc (24GBq) source, was obtained by elution of the 99Mo/99mTc

generator. The 99mTc was measured over 5 days and we measure 99mTc activity until reached values that were suitable with the measuring system, lowest resolution, as recommended by the manufacturer (0.2 for Capintec CRC-15R and 0.4 MBq for Capintec CRC-15PET).

Before taking any measurement, check that there are no radioactive sources that could interfere with the measurements. The dose calibrators are switched on 30 minutes before starting measurements. An activity was prepared in MBq of 99mTc slightly higher than the maximum activity that can be carried out with clinical and formal fines due to measures of the activities in the function in time until the activity of the farm was achieved.

The chosen approach for assessing the linearity of dose calibrator response concerning changes in source activities was the decay method. This method involves tracking the activity of 99mTc over time, allowing for the creation of a graph depicting the relationship between activity and time. By comparing the measurement activity values with the expected values for the same 99mTc at various measurement times, linearity can be evaluated. The overall inaccuracy for the sources examined in this study varied between ± 5% [39]. All materials and methods used are applicable to both calibrators, including processing for data analysis. To do this, were used the following materials:

- 99mTc;
- Capintec CRC-15R dose calibrator;
- Capintec CRC-15PET dose calibrator.

## B. Results and Discussion

The experiment included doing several measurements of the 99mTc source, it was seen that variations in their characteristics over a period were associated with the process of nuclear decay. All experimental measurements of Capintec CRC-15R and Capintec CRC-15PET are presented in table 1 and table 2 respectively. Thus, were used these data to determine the ratios and deviations seen between the measured and predicted activity of 99mTc source as well as their relationship in linear regression. The measurements were taken at various periods of time and places throughout the calibration adjustment process for Capintec CRC-15R and Capintec CRC-15PET. Note that first, we will present the results and discussion for Capintec CRC-15R dose calibrator and finally we will make analogy for Capintec CRC-15PET dose calibrator.

To establish the linearity connection between the measured activities and the predicted activities (the response), several time intervals were used to collect measurements of 99mTc activities. The Capintec CRC-15R results are shown in table 1.

Table 5.1. Shows the ratios and deviations seen between the measured and predicted activity of 99mTc source for Capintec CRC-15R.

| Days | Hour (hh:mm) | t (h) | $A_{mea}$ (MBq) | $A_{exp}$ (MBq) | $\Delta A_{abs}$ (MBq) | $\Delta A_{rel}$ (%) | $\Delta A_{reg}$ (MBq) | $\Delta A_{reg}$ (%) |
|---|---|---|---|---|---|---|---|---|
| dia 1 | 10:46 | 0 | 2.39E+04 | 2.39E+04 | 0.00E+00 | 0.0 | 2.39E+04 | -0.02 |
| | 11:56 | 1.17 | 2.09E+04 | 2.09E+04 | 1.04E+01 | 0.0 | 2.09E+04 | -0.02 |
| | 13:11 | 2.42 | 1.81E+04 | 1.81E+04 | -1.36E+01 | -0.1 | 1.81E+04 | -0.02 |
| | 14:24 | 3.63 | 1.57E+04 | 1.57E+04 | -4.87E+00 | 0.0 | 1.57E+04 | -0.02 |
| | 15:40 | 4.90 | 1.36E+04 | 1.36E+04 | 2.15E+00 | 0.0 | 1.36E+04 | -0.03 |
| | 16:49 | 6.05 | 1.19E+04 | 1.19E+04 | -3.04E+01 | -0.3 | 1.19E+04 | -0.03 |
| dia 2 | 9:19 | 22.55 | 1.77E+03 | 1.77E+03 | -4.29E+00 | -0.2 | 1.77E+03 | -0.09 |
| | 10:44 | 23.97 | 1.50E+03 | 1.50E+03 | -4.15E+00 | -0.3 | 1.50E+03 | -0.1 |
| | 11:46 | 25.00 | 1.33E+03 | 1.34E+03 | -2.07E+00 | -0.2 | 1.33E+03 | -0.12 |
| | 13:06 | 26.33 | 1.14E+03 | 1.14E+03 | -2.68E+00 | -0.2 | 1.14E+03 | -0.13 |
| | 14:39 | 27.88 | 9.57E+02 | 9.57E+02 | -2.05E-01 | 0.0 | 9.58E+02 | -0.15 |
| | 15:51 | 29.08 | 8.31E+02 | 8.33E+02 | -2.42E+00 | -0.3 | 8.32E+02 | -0.18 |
| | 16:58 | 30.20 | 7.32E+02 | 7.33E+02 | -6.62E-01 | -0.1 | 7.33E+02 | -0.2 |
| dia 3 | 9:08 | 46.37 | 1.13E+02 | 1.13E+02 | -4.23E-01 | -0.4 | 1.14E+02 | -1.18 |
| | 10:13 | 47.45 | 9.97E+01 | 1.00E+02 | -3.94E-01 | -0.4 | 1.01E+02 | -1.33 |
| | 11:29 | 48.72 | 8.62E+01 | 8.65E+01 | -2.82E-01 | -0.3 | 8.75E+01 | -1.53 |
| | 12:35 | 49.82 | 7.61E+01 | 7.62E+01 | -7.29E-02 | -0.1 | 7.74E+01 | -1.73 |
| | 14:04 | 51.30 | 6.40E+01 | 6.42E+01 | -1.89E-01 | -0.3 | 6.53E+01 | -2.04 |
| | 15:09 | 52.38 | 5.64E+01 | 5.66E+01 | -2.46E-01 | -0.4 | 5.77E+01 | -2.31 |
| | 16:29 | 53.72 | 4.84E+01 | 4.86E+01 | -1.68E-01 | -0.3 | 4.97E+01 | -2.68 |
| dia 4 | 9:47 | 71.02 | 6.70E+00 | 6.60E+00 | 1.03E-01 | 1.6 | 8.03E+00 | -16.5 |
| | 11:06 | 72.33 | 5.70E+00 | 5.67E+00 | 3.29E-02 | 0.6 | 7.03E+00 | -18.9 |
| | 12:30 | 73.73 | 4.91E+00 | 4.82E+00 | 8.83E-02 | 1.8 | 6.24E+00 | -21.3 |
| | 13:45 | 74.98 | 4.27E+00 | 4.17E+00 | 9.60E-02 | 2.3 | 5.60E+00 | -23.7 |
| | 15:00 | 76.23 | 3.72E+00 | 3.61E+00 | 1.07E-01 | 3.0 | 5.05E+00 | -26.3 |
| | 16:25 | 77.65 | 3.15E+00 | 3.07E+00 | 8.16E-02 | 2.7 | 4.48E+00 | -29.6 |
| | 17:36 | 78.83 | 2.78E+00 | 2.68E+00 | 1.03E-01 | 3.9 | 4.11E+00 | -32.3 |
| dia 5 | 9:35 | 94.82 | 3.00E-01 | 4.23E-01 | -1.23E-01 | -29.1 | 1.63E+00 | -81.5 |
| | 11:14 | 96.47 | 2.00E-01 | 3.50E-01 | -1.50E-01 | -42.8 | 1.53E+00 | -86.9 |
| | 12:31 | 97.75 | 2.00E-01 | 3.02E-01 | -1.02E-01 | -33.7 | 1.53E+00 | -86.9 |
| | 13:58 | 99.20 | 2.00E-01 | 2.55E-01 | -5.52E-02 | -21.6 | 1.53E+00 | -86.9 |
| $A_0$ [MBq] | | 23900 | | | | | | |
| $T_{1/2}$ (99mTc) [h] | | 6.0067 | | | | | | |

It is important to note that in table 5.1 and 5.2, the parameters are defined as: $A_{mea}$ is measured activity, $A_{exp}$ is expected activity, which is calculate using equation 5.3, $\Delta A_{abs}$ is absolute value of the activity, obtained by the difference between the measured value and the expected value. $\Delta A_{rel}$ is the relative value of the activity,

obtained calculated by the difference between the measured value and the expected value and divided by the expected value, then multiplied by 100%. $\Delta A_{reg}$ is absolute value of the activity in the linear regression model, which is calculated using equation 5.5 and $\Delta A_{reg}(\%)$ is activity deviation in the linear regression model. This value is obtained calculating the difference between the measured value and the value obtained in the linear regression model and divided by the linear regression model value, then multiplied by 100%. Figure 5.7 shows the relation between expected and measured activities as a function of time, for Capintec CRC-15R dose calibrator.

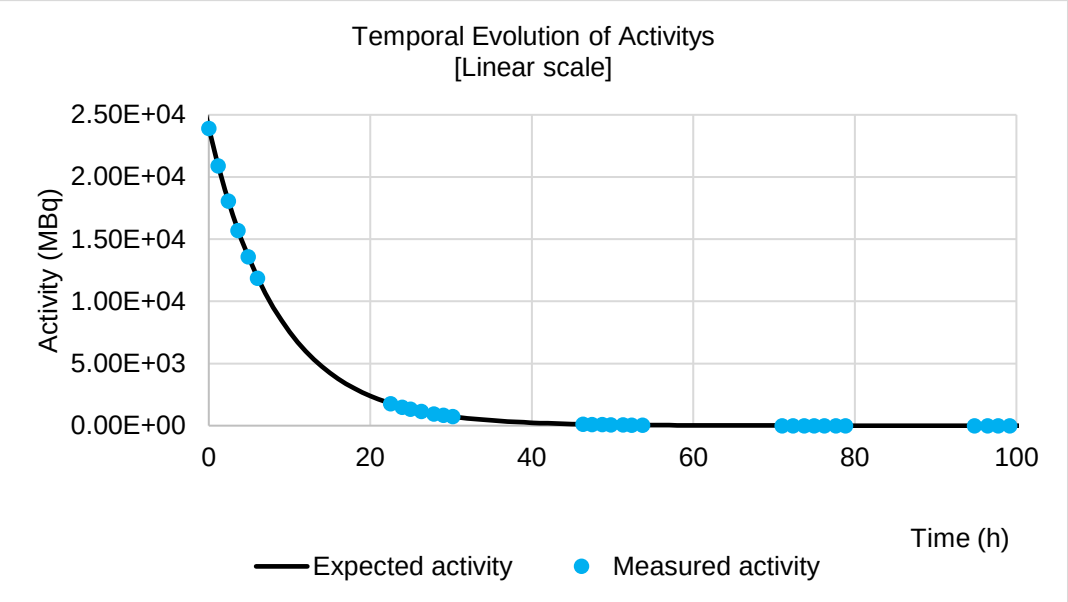


Figure 5.8. The graph shown above illustrates the phenomenon of exponential decay exhibited by the 99mTc source, specifically depicting the decline in activity as predicted by theoretical knowledge for Capintec CRC-15R dose calibrator.

The visualization of the points in the graph above is hindered using linear scale that is not conducive to optimal visualization, as well as the occurrence of overlapping points within the graph.

$$A_{exp}(t) = A_0 \times 2^{-\frac{t}{T_{1/2}}} \qquad \text{Equation 5.3.}$$

where $A_{exp}$ is expected activity, $A_0$ is initial activity, $T_{1/2}$ is half-life for 99mTc, t is the time. To better visualize figure 5.8, an alternative scale known as a logarithmic scale is used to present the data more effectively.

$$A_{exp}(t) = A_0 \times 2^{-\frac{t}{T_{1/2}}} \Leftrightarrow \log_2\left(\frac{A_{exp}}{A_0}\right) = -\frac{t}{T_{1/2}} \qquad \text{Equation 5.4.}$$

where half-life is given by: $T_{1/2}$ (99mTc) [h] = 6.0067

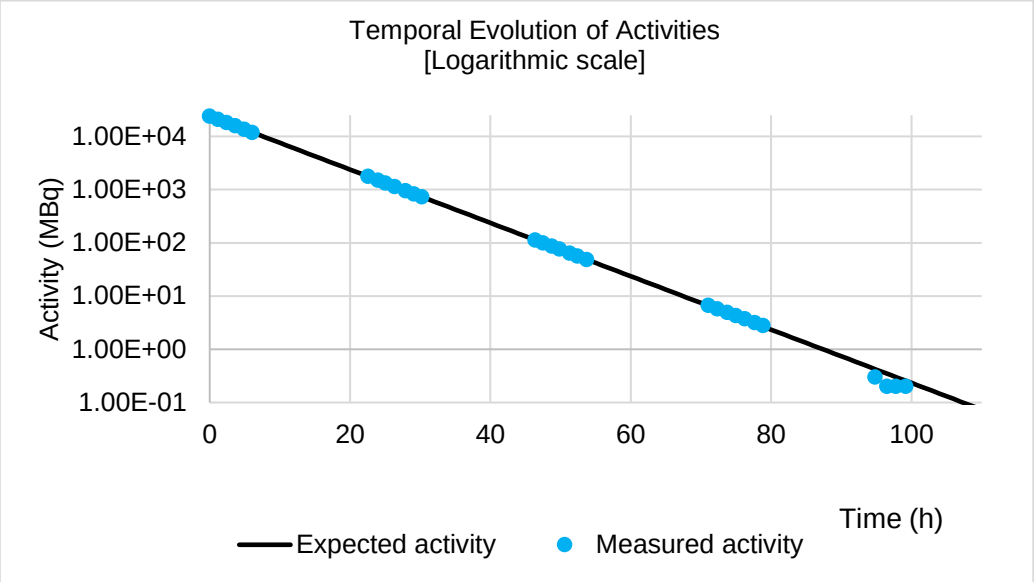


Figure 5.9. The graph shown above illustrates the phenomenon of exponential decay exhibited by the $99mT_c$ source between expected activity and activity measured on the logarithmic scale, for Capintec CRC-15R dose calibrator.

The last points illustrate the events occurring on the fifth day, when the decay progressively approaches a stable value of 0.2 MBq between 11:14 to 13:58. This indicates that the activity has reached its limit of decay. To enhance the examination of linearity, it was imperative to create a graphical representation that depicts the expected activities in relation to the measured activities. Additionally, it was essential to identify the potential regime location where linearity is present.

Once again, as described earlier, the first points illustrate the events occurring on the fifth day, when the decay progressively approaches a stable value of 0.2 MBq between 11:14 to 13:58. This indicates that the activity has reached its limit of decay. In this scenario, it is anticipated that these specific points would be omitted from our analysis in subsequent investigations, since they fail to provide any meaningful contribution to our research. It turned out that we could easily separate the overlapping points on the linear scale as seen in figure 1.9, proving that the linear connection does, in fact, hold.

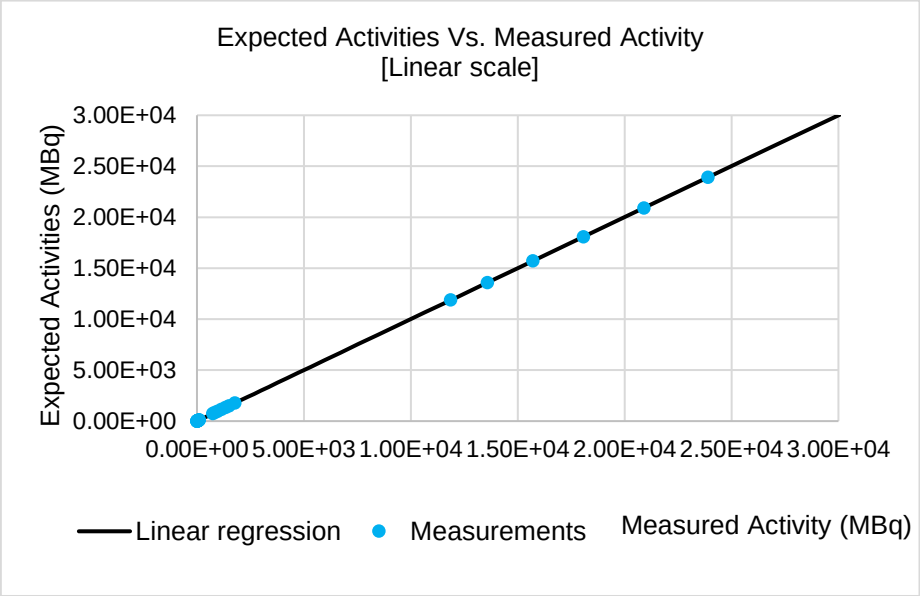


Figure 5.10. Shows the relationship between expected and measured activities in linear regression.

However, there is a robust correlation between observed and predicted behaviors. The linearity of actions shall thereafter be studied. In figure 5.10, we can better visualize the results using the logarithmic scale, as it allows the overlapping points to be separated.

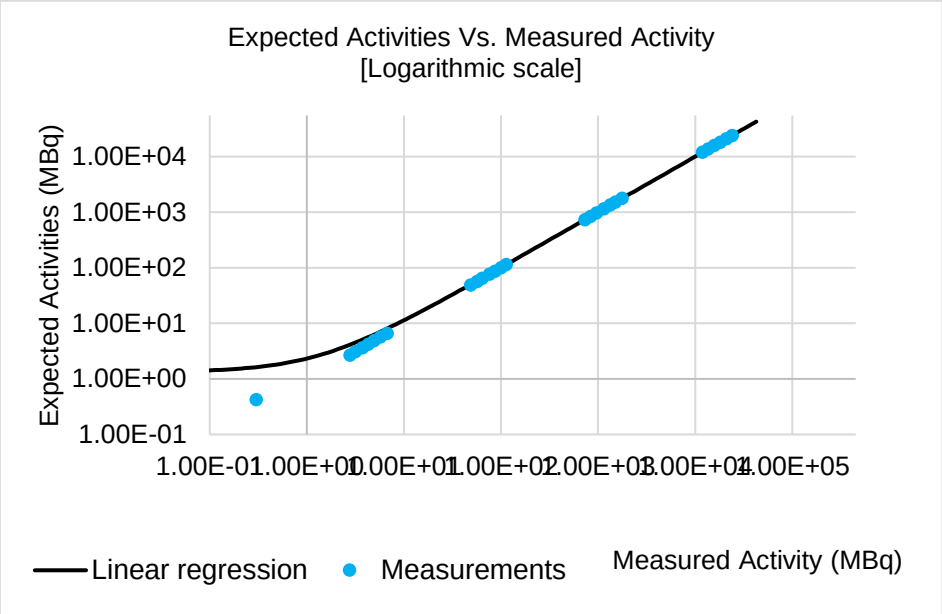


Figure 5.11. Shows a logarithmic scale relationship between expected and measured activities in linear regression.

So, we have a linear model that is extremely close to direct proportionality.

$$A_{exp}(A_{measured}) = m \times A_{measured} + b \begin{cases} m = 1.00 \pm 0{,}00 \\ b = 1{,}33 \pm 1.52\ (MBq) \end{cases}$$ Equation 5.5.

As previously stated, and shown, it has been established that the dose calibrator Capintec CRC-15R operates within a certain range where there is a linear relationship between the expected and measured activities. The presence of linearity is evident in the deviation graphs depicting the relationship between expected and measured activities. It is worth noting that some data points exhibit non-linearity, even when considering the deviation between expected activities and the linear model.

In figure 1.11, we can better visualize the results using the logarithmic scale. In this graph, we can verify that all points are within tolerance according to national legislation.

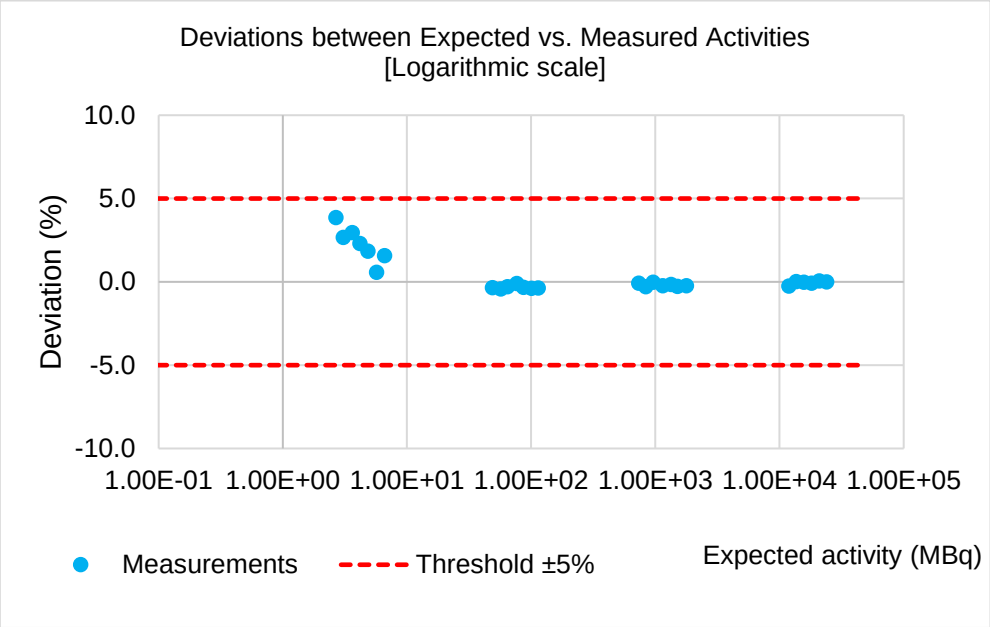


Figure 5.12. Shows the deviation of expected and measured activities whose threshold is ± 5%

In figure 5.12, we see when we use the expected activity x linear model, some values are out of tolerance. This fact happens because the dose calibrator has a certain interval range where it verifies linearity.

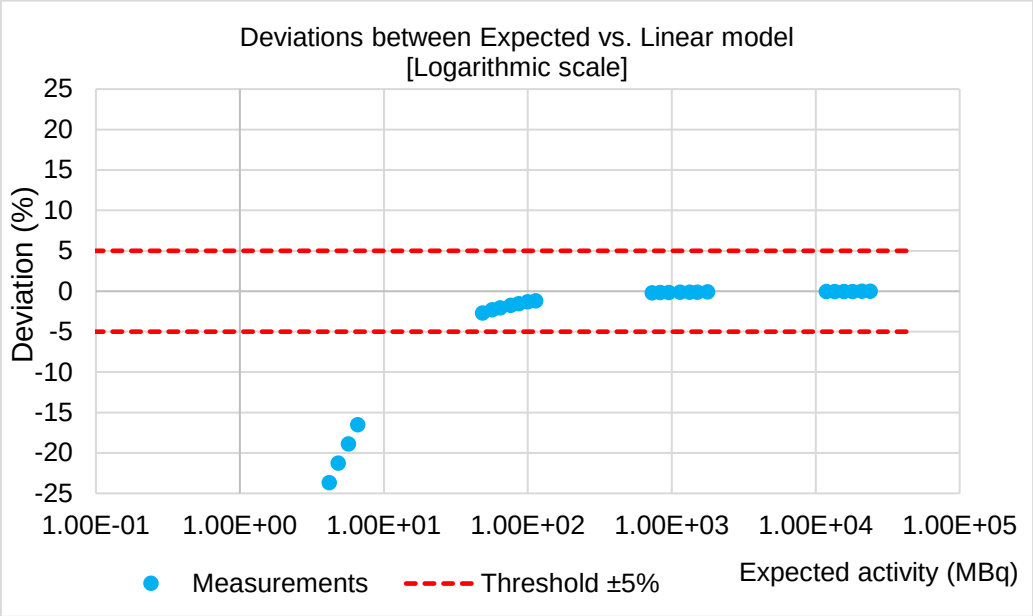


Figure 5.13. Shows the deviation of expected activity and linear model whose threshold is ± 5%

Based on figure 5.12, it is evident that the Capintec CRC-15R dose calibrator exhibits linearity throughout the range of 1.00E+02 to 1.00E+5 MBq, which corresponds to 1.00E+08 to1.00E+11 Bq.

For the Capintec CRC-15PET dose calibrator, the same measurement and data analysis procedures were carried out, similar to the previous case, making it possible to determine the equation that best describes the linearity relationship using the data in table 2.

Table 5.2. Shows the ratios and deviations seen between the measured and predicted activity of $^{99m}T_c$ source as well as their relationship in linear regression For the Capintec CRC-15PET

| Days | Hours (hh:mm) | t (h) | $A_{mea}$ (MBq) | $A_{exp}$ (MBq) | $\Delta A_{abs}$ (MBq) | $\Delta A_{rel}$ (%) | $\Delta A_{reg}$ (MBq) | $\Delta A_{reg}$ (%) |
|---|---|---|---|---|---|---|---|---|
| day 1 | 10:53 | 0.00 | 2.44E+04 | 2.440E+04 | 0.00E+00 | 0. 00 | 2.44E+04 | 0.08 |
| | 12:02 | 1.15 | 2.14E+04 | 2.137E+04 | 3.23E+01 | 0.15 | 2.14E+04 | 0.08 |
| | 13:16 | 2.38 | 1.86E+04 | 1.853E+04 | 2.69E+01 | 0.15 | 1.85E+04 | 0.08 |
| | 14:29 | 3.60 | 1.61E+04 | 1.611E+04 | 4.53E+00 | 0.03 | 1.61E+04 | 0.07 |
| | 15:45 | 4.87 | 1.39E+04 | 1.392E+04 | 1.47E+01 | 0.11 | 1.39E+04 | 0.07 |
| | 16:52 | 5.98 | 1.22E+04 | 1.223E+04 | 7.06E+00 | 0.06 | 1.22E+04 | 0.07 |
| day 2 | 9:24 | 22.52 | 1.81E+03 | 1.815E+03 | -5.31E+00 | -0.29 | 1.81E+03 | 0.00 |
| | 10:48 | 23.92 | 1.54E+03 | 1.545E+03 | -4.50E+00 | -0.29 | 1.54E+03 | -0.02 |
| | 11:50 | 24.95 | 1.37E+03 | 1.371E+03 | -5.89E+00 | -0.43 | 1.37E+03 | -0.03 |
| | 13:17 | 26.40 | 1.16E+03 | 1.160E+03 | -3.67E+00 | -0.32 | 1.16E+03 | -0.06 |
| | 14:36 | 27.72 | 9.92E+02 | 9.962E+02 | -4.21E+00 | -0.42 | 9.93E+02 | -0.08 |
| | 15:58 | 29.08 | 8.43E+02 | 8.509E+02 | -7.86E+00 | -0.92 | 8.44E+02 | -0.11 |
| | 17:08 | 30.25 | 7.37E+02 | 7.437E+02 | -6.69E+00 | -0.90 | 7.38E+02 | -0.13 |
| day 3 | 9:13 | 46.33 | 1.16E+02 | 1.162E+02 | -2.42E-01 | -0.21 | 1.18E+02 | -1.29 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 10:19 | 47.43 | 1.02E+02 | 1.024E+02 | -8.47E-02 | -0.08 | 1.04E+02 | -1.47 |
| | 11:33 | 48.67 | 8.86E+01 | 8.880E+01 | -2.03E-01 | -0.23 | 9.01E+01 | -1.71 |
| | 12:54 | 50.02 | 7.60E+01 | 7.599E+01 | 7.73E-03 | 0.01 | 7.76E+01 | -2.00 |
| | 14:09 | 51.27 | 6.58E+01 | 6.578E+01 | 1.53E-02 | 0.02 | 6.74E+01 | -2.32 |
| | 15:14 | 52.35 | 5.80E+01 | 5.805E+01 | -5.41E-02 | -0.09 | 5.96E+01 | -2.63 |
| | 16:35 | 53.70 | 4.96E+01 | 4.968E+01 | -7.94E-02 | -0.16 | 5.12E+01 | -3.08 |
| day 4 | 9:51 | 70.97 | 6.80E+00 | 6.774E+00 | 2.60E-02 | 0.38 | 8.41E+00 | -19.15 |
| | 11:11 | 72.30 | 5.90E+00 | 5.808E+00 | 9.20E-02 | 1.58 | 7.51E+00 | -21.46 |
| | 12:36 | 73.72 | 5.00E+00 | 4.932E+00 | 6.80E-02 | 1.38 | 6.61E+00 | -24.39 |
| | 13:50 | 74.95 | 4.40E+00 | 4.278E+00 | 1.22E-01 | 2.86 | 6.01E+00 | -26.83 |
| | 15:12 | 76.32 | 3.72E+00 | 3.654E+00 | 6.64E-02 | 1.82 | 5.33E+00 | -30.25 |
| | 16:31 | 77.63 | 3.20E+00 | 3.139E+00 | 6.14E-02 | 1.96 | 4.81E+00 | -33.53 |
| | 17:41 | 78.80 | 2.80E+00 | 2.743E+00 | 5.67E-02 | 2.07 | 4.41E+00 | -36.57 |
| day 5 | 9:40 | 94.78 | 4.00E-01 | 4.338E-01 | -3.38E-02 | -7.78 | 2.02E+00 | -80.16 |
| | 11:19 | 96.43 | 4.00E-01 | 3.586E-01 | 4.14E-02 | 11.56 | 2.02E+00 | -80.16 |
| | 12:36 | 97.72 | 4.00E-01 | 3.092E-01 | 9.08E-02 | 29.36 | 2.02E+00 | -80.16 |
| | 14:03 | 99.17 | 4.00E-01 | 2.616E-01 | 1.38E-01 | 52.92 | 2.02E+00 | -80.16 |
| $A_0$ (MBq) | | 2.44E+04 | | | | | | |
| $T_{1/2}$ [99mTc] (h) | | 6.0067 | | | | | | |

As previously case, for Capintec CRC-15PET dose calibrator, the linear regression model graph (figure 5.13) was obtained on the linear scale between the obtained and expected activities. This model was used to verify whether there is a linear relationship between the two quantities. The same line of thought was used in the Capintec CRC-15R dose calibrator.

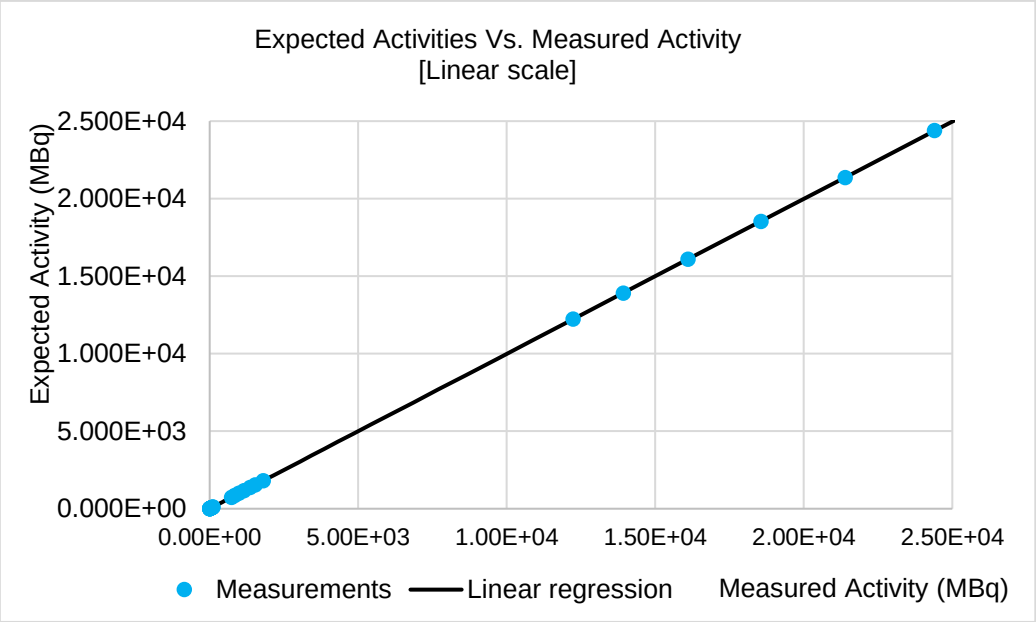


Figure 5.14 Shows the relationship between expected and measured activities in linear regression.

Thus, a linear model very close to direct proportionality was obtained:

$$A_{exp}(A_{measured}) = m \times A_{measured} + b \begin{cases} m = 0{,}99 \ \pm 0{,}00 \\ b = 1{,}62 \ \pm 1{,}24 \ (MBq) \end{cases} \quad \text{Equation 5.6}$$

However, deviations from the linearity regime were observed for measured activities: in the range less than 10 MBq. It now remains to graph the deviations between the expected activities and the activities obtained by the linear model.

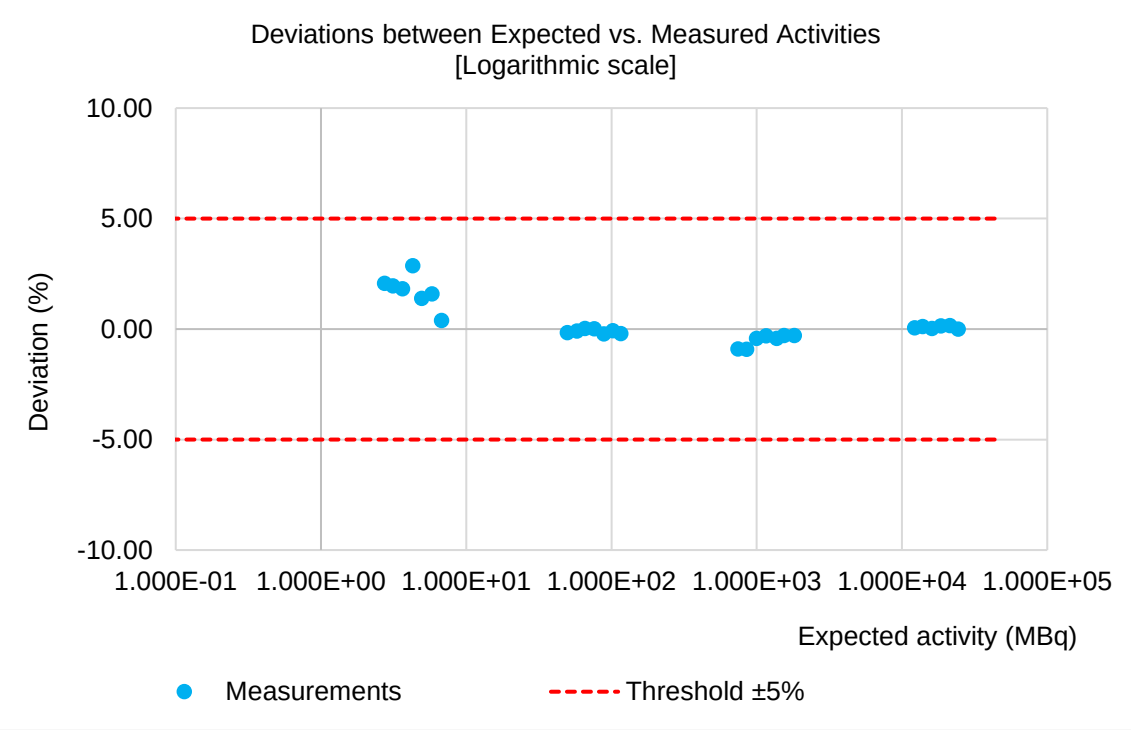


Figure 5.15. Shows the deviation of expected and measured activities whose threshold is ± 5%.

As we can see from the graph, the deviation points are within the acceptable range, in the case of expected activity and measured activity whose deviation is ± 5% [39].

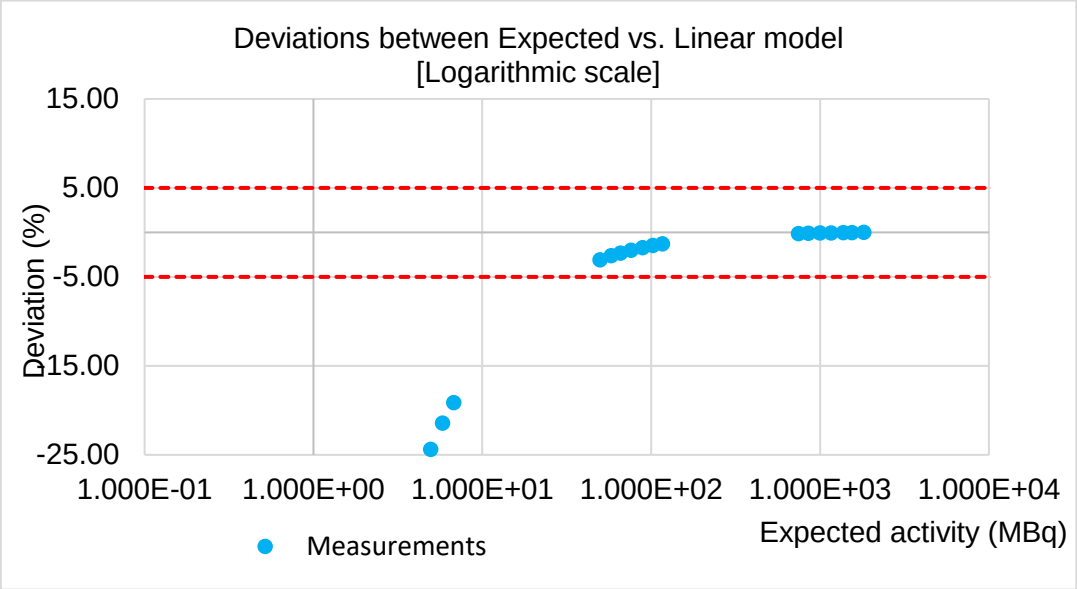


Figure 5.16. Shows the deviation of expected and measured activities whose threshold is ± 5%. In the latter case, we can see the deviations are below 10 MBq.

In this case, linearity can be seen to be below 10 MBq for Capinter CRC-15PET and dose calibrator Capintec CRC-15R exhibits linearity throughout the range of 1.00E+02 to 1.00E+5 MBq, which corresponds to 1.00E+08 to1.00E+11 Bq or linearity is seen to be above 100 MBq.

It should be noted that for both dose calibrators, an activity of 740 MBq of 99mTc was measured, which is the average activity for clinical use. This allowed us to make several measurements of the drop in activity as a function of time over 5 days until the activity reached the background level. For both dose calibrators we were able to verify that on the fifth day of measurement the activity values were outside the limits shown in figures 5.12 and 5.15. This fact is due to very low activity values close to zero that are outside the linearity range of the dose calibrators.

Thus, the calibrator response is considered linear when the ratio between the measured and predicted response remains constant over the range of currents for which the calibrator was produced. Therefore, dose calibrators obey linearity, allowing in this case the dose to be administered with precision for diagnosis and therapy for patient treatment. On the other hand, although there are deviations at some points along the line, the calibrators present a range in which they exhibit linearity, and which ensure dose measurement accurately measures the activity of a radioactive source within a range of values.

## 5.3.2. Gamma Camera: Extrinsic and intrinsic uniformity testing

Extrinsic uniformity measures the uniformity parameter under normal working conditions, that is, the image acquisition process is done with a collimator (low energy high resolution (LEHR) collimator for 99mTc), while the intrinsic uniformity of image acquisition occurs without a collimator. However, this protocol was applied for intrinsic uniformity and extrinsic uniformity tests as well as image analysis processing for different equipment.

### A. Materials and Methods

To carry out the extrinsic uniformity test, the following materials and methods were required:

- 99mTc flood source
- Gamma camera Philips Brightview;
- Gamma camera Millenium MG

It is important to stress that $99mT_C$ flood source is large enough to cover the entire field useful view of the detector. It must produce a rate lower than 20 kcps. The source is placed centrally area covers the entire useful field of view. The distance from the source to the collimator must be reproducible.

To carry out the intrinsic uniformity test, the following materials and methods were required:

- 99mTc point source
- Gamma camera Philips Brightview;
- Gamma camera Millenium MG

The $99mT_C$ point source must produce a rate lower than 20 kcps. The source is placed according to the manufacturer's instructions and the distance from the source to the collimator must be reproducible.

### B. Conditions of acquisition

i. Extrinsic uniformity:

- Radionuclide: 99mTc.
- Collimator: LEHR;
- Matrix size: 64 × 64;
- Number of accounts: at least 4000 kc must be registered in total;

- Acquisition window: 15% or as indicated by the manufacturer;
- Account rate ≈ 20 kcps.

ii. Intrinsic uniformity:

- Radionuclide: 99mTc;
- Collimator: not applicable;
- Matrix size: 64 × 64.
- Number of accounts: at least 4000 kc must be registered in total;
- Acquisition window: 15% or as indicated by the manufacturer;
- Account rate ≈ 20 kcps.

## C. Processing and analysis of results

To process and analyze the data, the following tools were used: *ImageJ, Plugins and Image Quantification code* developed using the Python programming language. Data from the three tools were compared with data provided by the manufacturer as well as compared with theoretical data from RP-162 which suggests that at most extrinsic and intrinsic uniformity should not exceed 7% [39].

**I.** **ImageJ**: is software initially developed by Wayne Rasband at the National Institutes of Health (NIH) for open-source image processing widely used in the scientific community for analyzing and processing medical images. It provides a comprehensive set of tools for tasks ranging from simple measurements to complex image analysis. To analyze the data through imageJ we first removed the edges of the images.

Edge pixels are removed as follows: All edge pixels in the UFOV that have less than 75% [47]of the average counts are assigned zero counts. Once this is done, the pixels that now have any of the four side pixels with a zero count are also set to zero. The image is smoothed by applying the 9-point filter.

| | | |
|---|---|---|
| 1 | 2 | 1 |
| 2 | 4 | 2 |
| 1 | 2 | 1 |

The weight factor for a pixel outside the analyzed area is zero. The smoothed value is found by dividing the pixel value by the sum of the non-zero factors. The **integral uniformity** of the UI is defined as the difference between the maximum and minimum

number of counts recorded per pixel in the study area divided by the sum of both and multiplied by one hundred.

$$IU = \frac{\max\_pixel\_count - \min\_pixel\_count}{\max\_pixel\_count + \min\_pixel\_count} \times 100\% \qquad \text{Equation 5.7.}$$

Differential uniformity is the maximum value of all those obtained by applying the previous formula to each set of 5 contiguous pixels in each row or column of the area under study.

$$DU = \frac{\text{high} - \text{low}}{\text{high} + low} \times 100\% \quad \text{Equation 5.8.}$$

The following values were calculated:

- Integral uniformity in the useful field of view (UFOV) and in the central field of useful vision (CFOV).
- Differential uniformity in UFOV and CFOV.

It should be noted that Useful Field of View (UFOV) is defined as the area of the detector used for imaging x-rays or gamma rays and is designated by the manufacturer. With the developed Python software, we were able to obtain the uniformized FOV later used in imageJ.

The images will be visually analyzed, varying the gray scale to better appreciate uniformity defects. The values obtained during processing are compared with the tolerances and with references. In the case of intrinsic uniformity, in which in this case the images are obtained without a collimator, the image processing procedures are the same. To obtain the number of maximum and minimum counts using imagJ, follow these steps:

- Insert image into ImagJ;
- Process;
- Filter;
- Convolution.

After that, from (equations 5.7 and 5.8) we calculated integral uniformity and differential uniformity for extrinsic and intrinsic uniformity. The results found are presented in table 5.3 and table 5.4.

## II. Image Quantification Code

***Python Image Quantification code*** is a code developed using the Python programming language to analyze and quantify DICOM images as integral and differential uniformity for UFOV and CFOV in images with extrinsic and intrinsic uniformity. To do this, the FOV was defined and then a filter was applied [46]:

$$\begin{matrix} 1 & 2 & 1 \\ 2 & 4 & 2 \\ 1 & 2 & 1 \end{matrix}$$

Where:

- FFOV (Full Field Of View) = 100% of image [47];
- UFOV (Useful Field Of View) = 95% of image [47];
- CFOV (Center Field Of View) = 75% of image [47].

After inserting the DICOM image, the Python Image Quantification allows you to cut the edges to eliminate zero pixels, defining the Full Field Of View (FFOV) that corresponds to 100% of the image. Using FFOV, we can define Useful Field Of View (UFOV) that corresponds to 95% of the image and Center Field Of View (CFOV) corresponds to 75% of the image.

Once this was done, we were able to calculate the integral and differential uniformity automatically using equations 5.7 and 5.8. The results are presented in tables 5.1 and 5.2. Detailed software script is in the attachment. Note that the UFOV and CFOV used in this software are the same as those used in ImageJ.

## III. Plugins

**Plugins** is the biggest integrated feature of ImageJ, which uses all the features of the Java language, such as ImageJ Application Programming Interface (ImageJ-IPA). This opens up a wide range of possibilities of what can be done in a plugin like filters perform image analysis or processing. ROI Manager defines regions where we want to evaluate uniformity. In our case, the ROIs were defined by Python and later used also in the plugins to analyze the integral and differential uniformities. This allowed us to obtain ROIs of the same size in all images acquired for different equipment.

Table 5.3. Philips Brightview: Extrinsic uniformity

| Extrinsic uniformity | | | Equipment | ImageJ | Plugins | Python |
|---|---|---|---|---|---|---|
| Det1 | UFOV | Integral uniformity | 4.52 | 5.66 | 4.85 | 3.67 |
| | | Differential uniformity | 2.39 | 4.16 | 3.01 | 2.85 |
| | CFOV | Integral uniformity | 3.88 | 3.00 | 2.85 | 2.28 |
| | | Differential uniformity | 2.39 | 2.69 | 2.54 | 2.85 |
| Det2 | UFOV | Integral uniformity | 4.26 | 5.19 | 4.07 | 3.23 |
| | | Differential uniformity | 2.48 | 2.37 | 3.7 | 2.27 |
| | CFOV | Integral uniformity | 4.03 | 2.36 | 2.22 | 2.22 |
| | | Differential uniformity | 2.00 | 2.80 | 2.03 | 2.03 |

Table 5.4. GE Millenium MG: Intrinsic uniformity

| Extrinsic uniformity | | | Equipment | ImageJ | Plugins | Python |
|---|---|---|---|---|---|---|
| Det1 | UFOV | Integral uniformity | 5.03 | 16.59 | 14.16 | 11.21 |
| | | Differential uniformity | 2.43 | 13.77 | 12.66 | 13.46 |
| | CFOV | Integral uniformity | 4.14 | 14.29 | 10.34 | 11.21 |
| | | Differential uniformity | 2.07 | 12.22 | 10.34 | 13.46 |
| Det2 | UFOV | Integral uniformity | 4.70 | 16.59 | 11.61 | 11.41 |
| | | Differential uniformity | 2.69 | 13.23 | 11.11 | 11.52 |
| | CFOV | Integral uniformity | 4.00 | 14.28 | 9.59 | 10.50 |
| | | Differential uniformity | 2.00 | 13.39 | 8.7 | 11.21 |

The results found and presented in tables 5.3 and 5.4, we were able to verify that the values of integral and differential uniformity are in accordance with the values

provided by the manufacturer and this also with the tolerances of allowed values are 7% for the three image analysis methods. It is noted that in the case of the developed software it provides satisfactory results, and it is also seen in certain cases that the Plugin developed by Java and the software can provide equal results and in others there is a millimetric difference. This allows us to conclude that the developed software satisfies the requirements and purposes of its development.

### 5.3.3. Gamma Camera: Sensitivity

Planar sensitivity determines the efficiency of the detectors. Constant fluctuations in the efficiency of detectors, such as photomultiplier tubes (PMTs) in scintillation cameras across the camera ranges, can cause differences in sensitivity. This may be due to wear on the detectors, temperature variations or even manufacturing defects.

#### A. Materials and Methods

A background image was obtained for each head for a minimum of 1 minute. For planar sensitivity phantom was placed above collimator, in the center of the Center Field Of View (CFOV). At the time of data acquisition, data were noted, namely activity, acquisition time, as well as background (without origin) and was subsequently subtracted during data analysis. The expression for the sensitivity calculation is given as follows, as suggested in the IEC [14] and NEMA [47] standards.

#### B. Conditions of acquisitions

- Radionuclide: 99mTc,
- Collimator: LEHR;
- Matrix size: 512 X 512;
- Number of accounts: 2500 kc;
- Account fee: less than 20 kcps;
- Acquisition window:15%.
- Phantom: Sensitivity phantom.

#### C. Processing and Analysis of results

Detection sensitivities are obtained by dividing the count value (minus the background count) by the source activity (corrected for decay) and the mean and variance between them are analyzed for each detector. For each of the acquisitions, sensitivity is calculated using the following equation:

$$S_i = \frac{C_i}{t_i A_i} \qquad \text{Equation 5.9.}$$

Where $S_i$ is the sensitivity, $C_i$ is the count, $A_i$ activity and $t_i$ is acquisition time. To determine contact activity, the average of the 4 values obtained was calculated (one per quadrant). The value obtained was compared with that specified by the manufacturer. Here, Counts: is count with background, Cts w/o back: is count without background, cps: is count per secund, and Aq is acquisition activity.

Table 5.5. Siemens Symbia pro.specta: sensitivity

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1st measure (5ml syringe) | | | 1.42 (mCi) | | 52.54 (MBq) | | |
| Hour | | | 15:00 (h) | | | | |
| Rest (5ml syringe) | | | 0.28 (mCi) | | 10.21 (MBq) | | |
| Hour | | | 15:10 (h) | | | | |
| Rest (50 ml syringe) | | | 0.06 (mCi | | 2.33 (MBq) | | |
| Hour | | | 15:17 | | | | |
| Phantom activity | | | 1.08 (mCi) | | 39.99(MBq) | | |
| Acquisition time | | | 10 min | | | | |
| Results | | | | | | | |
| Det 1 | Hour | Aq(MBq) | Background | Counts | Cts w/o back | cps | cps/MBq |
| | 16:13 | 34.79 | 3909.87 | 2786233.56 | 2782323.69 | 4637.2 | 133.29 |
| Det 2 | Hour | Aq(MBq) | Background | Counts | Cts w/o back | cps | cps/MBq |
| | 16:27 | 33.74 | 2970.89 | 2774844.38 | 2771873.49 | 4619.79 | 136.92 |

The data in tables 5.5 present the optimal sensitivity for both detectors, namely 133.29 for detector 1 and 136.92 cps/MBq for detector 2. Thus, both detectors differ by 2.7%. The difference in sensitivity between the two detectors is acceptable and can be used without a problem for clinical purposes, and the difference in maximum sensitivity tolerance between the two detectors is 5%.

Table 5.6. Philips Brightview: sensitivity

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1st measure (5ml syringe) | | | 1.42 (mCi) | | 52.54 (MBq) | | |
| Hour | | | 15:00 (h) | | | | |
| 2nd measure (5ml syringe) | | | 0.28(mCi) | | 10.21 (MBq) | | |
| Hour | | | 15:10 (h) | | | | |
| Rest (50ml syringe) | | | 0.06 | | 2.33 (MBq) | | |
| Hour | | | 15:17 | | | | |
| Phantom activity | | | 1.08 (mCi) | | 39.99(MBq) | | |
| Acquisition time | | | 10 min | | | | |
| Results | | | | | | | |
| Det 1 | Hour | Aq(MBq) | Backg | Counts | Cts w/o back | cps | cps/MBq |
| | 15:37 | 37.29 | 4978.69 | 2187836.94 | 2182858.25 | 3638.09 | 97.56 |
| Det 2 | Hour | Aq(MBq) | Backg | Counts | Cts w/o back | cps | cps/MBq |
| | 15:50 | 36.39 | 4616.03 | 2062668.06 | 2168052.03 | 3613.42 | 99.30 |

Furthermore, both detectors of the Philips Brightview exhibit relatively low sensitivity when compared to the Siemens Symbia pro.specta equipment. This is due to the natural decrease in detector sensitivity over time. For the Symbia pro.specta gamma camera, the sensitivity between the two detectors differs by only 1.8%.

Exact sensitivity values may vary depending on the test protocol, the collimation used (parallel, pinhole, etc.), and the radionuclide being detected (generally Tc-99m is used for sensitivity testing). However, for Philips BrightView as well as Siemens Symbia Pro.SPECTa, with the Technetium-99m (Tc-99m) radionuclide, typical sensitivity values are: No collimator (to test the raw detector): Can vary but is on the order of 200 to 300 cps/MBq (counts per second per megabecquerel). With high resolution (HR) collimator: Approximately 150 to 200 cps/MBq for the Tc-99m. With low energy collimator (LEGP - Low Energy General Purpose): Sensitivity tends to be higher, reaching around 180 to 220 cps/MB. These values differ from those presented in the tables 5.5 and 5.6 of this work because our equipment is old.

### 5.3.4. Gamma Camera: Deadtime measurements in scintillation camera

Reading time measurements in a scintillation chamber are essential to ensure accurate quantification of radioactivity in nuclear medicine. Therefore, there is an

important parameter in the scintillation chamber called deadtime. Thus, deadtime refers to the period after each detection event during which the system is unable to register another event. This can lead to underestimation of the true count rate, especially at high levels of activity.

### A. Materials and Methods

Two sources of 10 ml of 99mTc with an activity of 370 MBq (10 mCi) were required, which generate a counting rate of around 20 kcps in the equipment. The difference in activity between the two sources must not be greater than 10%. It is also necessary to use an Adams phantom (figure 5.16) to carry out this test. Dead time measurements were performed on the gamma camera Siemens Symbia pro.specta.

## B. Conditions of acquisition

- Radionuclide: used at the source (99mTc);
- Acquisition window: the one used in clinical applications of the radionuclide used in the source;
- Matrix: 512x512;
- Collimators: LEHR;
- Acquisition time per detector: 100 seconds;
- Number of counts: >1000 kcps;
- Counting rate: ± 20 kcps.

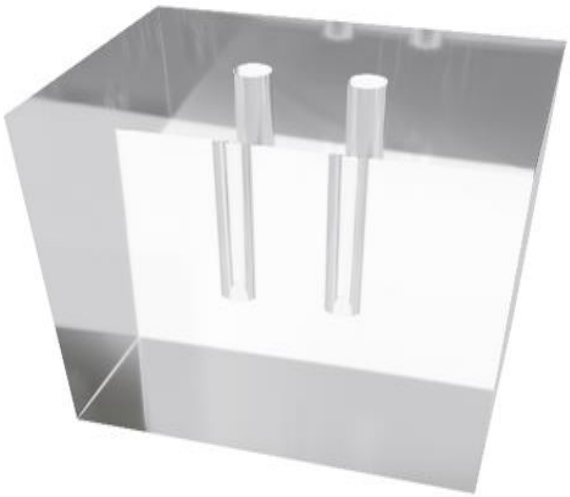

Figure 5.17. Adams Phantom (Pro-NM DualSource)

We used a LEHR collimator (99mTc), the Adams phantom which was placed in the center and in contact with the detector in a vertical position (90º or 270º) on the side of the thinnest wall.

Measurements were taken for 100 seconds which guarantees a count of the order of $10^6$ counts. Initially, a measurement of the bottom was carried out, and repeated at the end of the test. For all measurements, the following parameters were recorded: the counts obtained, the count rate and the time at which the various measurements were taken.

The two sources and two holes of the Adams phantom were properly identified as Source 1 and Source 2, Hole A and Hole B. After measuring the bottom, Source 1 was placed in hole A and a measurement was taken. Then, Source 2 was placed in hole B and a measurement was made with both sources inserted into the phantom. The third measurement must be carried out only with Source 2 in hole B. Finally, Source 2 was placed in hole A and a measurement was taken. The entire measurement process previously described was repeated with the inversion of the positioning of the sources.

## C. Processing and Analysis of results

The deadtime was determined using the expression (IAEA-TECDOC-602S), which can be used if the system responds to the penalizable model [46].

$$\tau_p = \frac{2\,OCR_{12}}{(OCR_1+OCR_2)^2} ln \frac{(OCR_1+OCR_2)}{2OCR_{12}} \qquad \text{Equation 5.10}$$

where $OCR_1$ and $OCR_2$ represent the net count rate for Source 1 and Source 2 respectively and $OCR_{12}$ the net count rate for the measurement with the two sources together. The count rate observed in the measurement in *i* ($OCR_i$), which corrects the count rate of measurement i for the decay during the time it lasts, is calculated with the expression [46]:

$$OCR_i = \frac{C_i.\ln(2)}{T_{1/2}\,.\,\{1-\exp((-\Delta t_i).\,\ln(2)/T_{1/2})\}} \qquad \text{Equation 5.11}$$

where $T_{1/2}$ is the half-life of (99mTc) expressed in seconds since measurement times are recorded in seconds. The counts for each measure will be corrected by the background:

$$C_i = C_{ti} - R_{bkg} \,.\, \Delta t_i \qquad \text{Equation 5.12.}$$

$C_{ti}$ are counts obtained in the measurement that starts at time $t_i$, where $R_{bkg}$ is the rate of background counts and $\Delta t_i$ is the duration of the measurement.

The incident count rate $ICR_i$ is obtained by correcting the rate observed in measurement $i$ by the time elapsed since the start of measurements according to the expression:

$$ICR_i = OCR_i \,.\, \exp\{\frac{(t_n - t_i)\,.\ln(2)}{T_{1/2}}\} \quad \text{Equation 5.13}$$

The rate of observed counts with a 20% loss can also be determined as:

$$OCR_{20} = 0{,}8\,.\,ICR_i$$

If the system, however, responds to an uninterrupted system, the expression for dead time would be given by [48]:

$$\tau_{np} = \frac{OCR_1.OCR_2 - \sqrt{OCR_1.OCR_2(OCR_{12} - OCR_1)(OCR_{12} - OCR_2)}}{OCR_1.OCR_2.OCR_{12}}$$

Therefore, the rate of accounts with losses of 20% would be given by the expression:

$$OCR_{20\%} = \frac{1}{4\tau_{np}}$$

Variations in the values of these parameters obtained in periodic tests must not differ by more than 20% from those in the reference test. The OCR20% and ICR20% values must be lower than those obtained with the intrinsic test.

## D. Results and discussion

After taking the measurements, data from different counts were obtained for detector 1 and detector 2. With this data was necessary to determine the deadtime.

Table 5.7. data obtained through detector 1.

| Image Name | Counts (kc) | Acquisition Time(s) | $R_{bkg}$ (kcps) | $C_i$ (kc) | $OCR_i$ (kcps) | Assembly |
|---|---|---|---|---|---|---|
| **IM1** | 3.58 | 120.00 | 0.03 | 0.045 | 0.00 | A0\|B0 |
| **IM2** | 976.14 | 76.67 | Na | 973.89 | 12.72 | A1\|B0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **IM3** | 972.82 | 38.41 | Na | 971.69 | 25.31 | A1\|B2 |
| **IM4** | 976.53 | 75.08 | Na | 974.33 | 12.99 | A0\|B2 |
| **IM5** | 975.24 | 75.79 | Na | 973.01 | 12.85 | A2\|B0 |
| **IM6** | 971.61 | 38.82 | Na | 970.47 | 25.02 | A2\|B1 |
| **IM7** | 975.98 | 77.83 | Na | 973.69 | 12.52 | A0\|B1 |
| **IM8** | 3.49 | 120.00 | 0.03 | -0.05 | -0.00 | A0\|B0 |

Table 5.8 shows the obtained count values and dead time with detector 1.

| | |
|---|---|
| $R_{bkg}$ (cps) | 30 |
| $OCR_1$ (cps) | 12622.26 |
| $OCR_2$ (cps) | 12922.62 |
| $OCR_1 + OCR_2$ | 25544.88 |
| $OCR_{12}$ (cps) | 25165.04 |
| $\tau_p$ (μs) | 1.16 |

Table 5.9. Data obtained through detector 2.

| Image Name | Counts (kc) | Acquisition Time(s) | $R_{bkg}$ (kcps) | $C_i$ (kc) | $OCR_i$ (kcps) | Assembly |
|---|---|---|---|---|---|---|
| **IM1** | 3.50 | 120 | 0.03 | -0.06 | -0.00 | A0\|B0 |
| **IM2** | 997.46 | 76.67 | Na | 995.17 | 12.99 | A1\|B0 |
| **IM3** | 999.29 | 38.41 | Na | 998.16 | 26.00 | A1\|B2 |
| **IM4** | 1001.07 | 75.08 | Na | 998.84 | 13.32 | A0\|B2 |
| **IM5** | 997.56 | 75.79 | Na | 995.30 | 13.15 | A2\|B0 |
| **IM6** | 999.22 | 38.82 | Na | 998.06 | 25.73 | A2\|B1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **IM7** | 1000.99 | 77.83 | Na | 998.68 | 12.85 | A0\|B1 |
| **IM8** | 3.63 | 120.00 | 0.03 | 0.06 | 0.00 | A0\|B0 |

Table 5.10. Shows the obtained count values and dead time with detector 2.

| | |
|---|---|
| $R_{bkg}$ (cps) | 30 |
| $OCR_1$ (cps) | 12922.0 |
| $OCR_2$ (cps) | 13233.3 |
| $OCR_1 + OCR_2$ | 26155.3 |
| $OCR_{12}$ (cps) | 25865.5 |
| $\tau_p$ (μs) | 0.843 |

The data obtained for the two detectors have the same order of magnitude and also differ by just one hundredth in deadtime for $Det_1$ is 1.16 μs and $Det_2$ is 0.843 μs, which shows the occurrence in the results for the two detectors.

## 5.3.5. Accreditation of PET/CT equipment

The main aim is to standardize the performance of 18F and 68Ga PET/CT in the acquisition of diagnostic images to minimize the effect of most technical factors that affect SUV variability, according to the European Association for Research Limit. Finally, analyze and compare the images obtained using the 18F PET/CT and 68Ga PET/CT with the images recommended by the European Association for Research Limit.

### 1. Calibration QC 18F PET/CT

### A. Materials

To do this experimental test was used materials for accreditation of 18F PET/CT in image acquisition, namely:

- Cylinder phantom with a diameter of approximately 20 cm;
- Water;
- Cylindrical homogeneity;
- Dose calibrator;
- A syringe with an activity of 18F that is accurately known. The activity now of measurement should be greater than 30 MBq but less than 100 MBq, ideally such that it will degrade to about 70 MBq at the anticipated time of phantom capture.

## B. Preparation

- We inject the 18F from the syringe into the uniformity phantom and flush it several times to ensure that the activity is transmitted into the phantom and measured the remaining activity in the empty syringe. Also, we registered the measurement time for activity in syringe;
- In addition, we fill the uniformity phantom entirely with water;
- Finally, we close the phantom and vigorously shake it to homogenize the activity.

## C. Procedures

- We put the phantom in the center of the field of view (FOV) on the scanner bed and utilized the standard of care patient scan settings, carry out scout and low dose CT for attenuation correction;
- We then obtain a PET/CT scan for each bed position for a minimum of two beds at a rate of 5min/bed and convert the speed when utilizing continuous bed motion to get parameters that are same for two beds at 5 min/bed. The acquisition parameters for the remaining portions of the scan should be set up as closely as feasible to the clinical acquisition protocol;
- Finally, we register the time when the PET series acquisition begins and include it in the scan report form when uploading the data via the EARL;

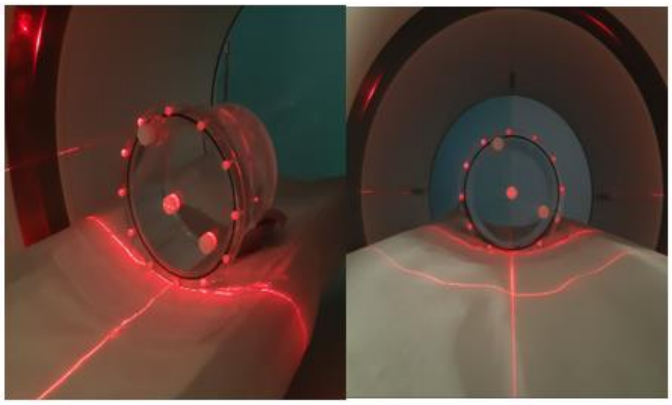

Figure 5.18. illustrates the cylindrical phantom and laser light used to better position the phantom.

## 2. Image quality control

### A. Materials

- A bottle to measure 1000 ml of stock solution;
- A dose calibrator;
- water or distilled water;
- Body image phantom of NEMA IEC caliber. Before filling the phantom, we inserted the lung if one is included. Without any water, polystyrene beads should be used to fill the lung insert. By increasing size in one axial plane, we must make sure that all the spheres are arranged sequentially;
- Long needle syringe for injecting stock solution into the spheres: to fill the spheres without damaging them, we use a needle that must be blunt and at least 15 cm long. Faster bead filling is possible thanks to a large volume syringe;
- Two syringes totaling 5 ml with 18F activity that is exactly known: when the anticipated phantom acquisition time comes around, each syringe activity of 18F should be such that it will degrade to about 20 MBq.


Figure 5.19. NEMA IEC body phantom with 18F

**B. Preparation of NEMA IEC body phantom**

The solution containing spheres, which contains approximately 20 kBq/ml:

- We fill precisely 1000 ml of water into the bottle and inject the 18F from one of the syringes into the bottle, flushing it several times to ensure the activity is transmitted into the bottle. We measure the remaining activity in the syringe that is empty and homogenized the solution in the bottle;
- Using the long, blunt needle from the syringe, we inject the homogenized solution into each of the spheres, making sure there are no air bubbles inside;
- After shaking the phantom vigorously, we closed it to ensure that the activity was evenly distributed throughout the background compartment;
- We used the scanner lasers to position the phantom on the scanner bed in the center of the field of view (relative to the gantry in both the horizontal and vertical directions);
- Finally, we use the standard of care patient scan settings to carry out scout and low dose CT for attenuation correction (CTAC).

**3. Materials for 68Ga PET/CT**

**A. Materials**

- Dose calibrator
- Water or distilled water
- Cylindrical Phantom with length sufficient to span the entire axial FOV of the scanner.

**B. Preparation**

- We inject the 68Ga syringe with exact and previously known activity measurements. By the time of the anticipated phantom acquisition, 68Ga activity should be such that it will degrade to about 37 MBq.
- After measuring the entire syringe, we injected the 68Ga activity into the phantom and repeatedly rinsed the syringe to make sure the activity was transmitted to the phantom and verified the syringe residual activity and shut the container and vigorously shake it to evenly distribute the activity.

**C. Procedures**

- We put the phantom on the scanner bed in the center of the field of view and obtain a PET/CT scan that includes a minimum of two bed positions lasting at

least five minutes each. The remaining scan acquisition parameters must be set up as closely as feasible to your 68Ga clinical acquisition methodology.

- We register the time when the PET series acquisition begins and include it in the scan report form when uploading the data via the EARL.

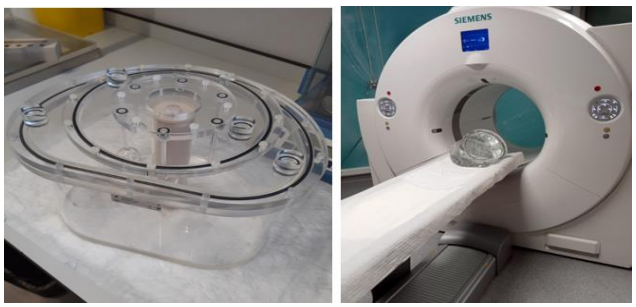


Figure 5.20. NEMA IEC body phantom with 68 Ga

In this chapter, we presented the data obtained during the accreditation of 18F PET/CT and 68Ga PET/CT as well as discussion. To start with results, we will deduce and analyze a useful expression that will be used in PET/CT accreditation and that will also allow us to calculate the final activity during the activity decay and in the subsequent discussion of the results. The equation to calculate activity is given:

$$A(t) = A_0 e^{-\lambda_p (t_{aq} - t_{meas})} \quad \text{Equation 5.14}$$

where, $t_{aq}$ is acquisition time and $t_{meas}$ is measurement time, $A(t)$ is activity for any instant and $A_0$ activity for instant t=0. We use the equation (5.13) to calculate the decay of activity.

Table 5.11. 18F PET/CT data table for cylinder

| | |
|---|---|
| $t_{meas}$(h) | 13:05 |
| $t_{aq}$(h) | 15:08 |
| $t_{meas} - t_{aq}$(min) | 123.0 |
| $\lambda_F$ (min) | 109.7 |
| $A_0$(MBq) | 143.0 |

using equation (5.14), we can determine the decay of the activity of 18F: $A(t = 123) = 65.7Mbq$. As we can see, decay activity corresponds to the expected activity which is at 70 MBq which is the value suggested by the European Association for Research Limit-EARL. In our case, we obtain a decay activity of 65.7 MBq, which is a satisfactory value, as it is very close to the value recommended by EARL.

Table 5.12. 18F PET/CT data table for NEMA IEC body phantom (sphere)

| | |
|---|---|
| $t_{meas}$(h) | 13:09 |
| $t_{aq}$(h) | 15:44 |
| $t_{meas} - t_{aq}$(min) | 155.0 |
| $\lambda_F$(min) | 109.7 |
| $A_0$(MBq) | 52.4 |

As in the previous case, the decay activity value is close to the expected value of 20 MBq as referenced by EARL. However, this case is much closer, with the activity value being 19.7 MBq.

Table 5.13. 18F PET/CT data table for bottom

| | |
|---|---|
| $t_{meas}$ (h) | 13:12 |
| $t_{aq}$ (h) | 15:44 |
| $t_{meas} - t_{aq}$ (min) | 152.0 |
| $\lambda_F$(min) | 109.7 |
| $A_0$(MBq) | 51.6 |

This is a similar case to the previous one, with the activity value obtained is 19.7 MBq and the expected value being 20 MBq. This is justified by the fact that the initial activities and measurement times do not differ much.

Table 5.14. 68Ga PET/CT data table for NEMA IEC body phantom

| | |
|---|---|
| $t_{meas}$(h) | 11:30 |
| $t_{aq}$(h) | 14:00 |
| $t_{meas} - t_{aq}$(min) | 150.00 |
| $\lambda_F(\min)$ | 67.71 |
| $A_0$(MBq) | 170.40 |

The PET/CT quantification tests with 68Ga and 18F, images were acquired with activities of 36.7 MBq and 70 MBq respectively, with the aim of obtaining EARL certification. This certification ensures that studies acquired on different equipment are interchangeable and quantification information is comparable. It is necessary to establish a strategy for harmonizing standard uptake value (SUV) quantification. This test is important because it provides quantitative information of glucose metabolism in organs and the factors that affect SUV as imaging biomarkers. Through this process, we verified that the calibration factor of the PET equipment corresponds to the calibration factor of the dose calibrator.

# CHAPTER VI

This chapter presents conclusions on quality assurance results in nuclear medicine based in International Atomic Energy Agency (IAEA) and International Commission on Radiation Protection (ICRP) as well as future work.

## 6. Conclusion and future work

Quality assurance in Nuclear Medicine based on the International Atomic Energy Agency (IAEA) and the European Commission (EC) are very similar. Therefore, both the IAE and the EC provide guidelines and recommendations for good radiation practices and radioactive substances, this is the common point between both. Despite this convergence, they differ in two main moments, namely in scope and implementation models. The IAEA supply international standards and guidelines for the use and management of radioactive substances and radiation in its member states in the world and provide a huge topic such as nuclear safety, security, safeguards and radiation protection in industry and medial exposure. The IAEA´s recommendations are applicable globally and supply a framework that member states can follow and adapt to their specific national regulations. Although these regulations and guidelines are supported by IAEA its implementation is not mandatory for their member states. The IAEA´s recommendations and guidelines address frameworks adaptable to different region or national context in order to emphasis on international cooperation and support.

European Commission (EC) scopes include Directives and regulations according to EU law. Thus, European Commission recommendations are directed at the European Community and emphasis on harmonizing radiation protection and nuclear safety standards across Europe to guarantee high levels of safety and environment protection. Also supply very detailed and specific requirements, with quantitative limits and mandatory according to their criteria. EC provides Directives such as Council Directive 2013/59/EURATOM of 5 December 2013 laying down basic safety standards for protection against the dangers arising from exposure to ionizing radiation. In general, European Commission's recommendations is mandatory and must be applicable with specific legal requirements that must implemented by European Union member states, ensuring that all relevant issues are addressed with high degree of uniformity and enforceability within the EU.

In the case of Mozambique, where nuclear medicine is still a dream, for its implementation it will be necessary to translate the recommendations of the IAEA and EC and adapt it to the country's realities. To achieve this, it will be necessary to train more national staff to bring this to fruition, followed by the creation of national laws and standards, specifying in detail the qualifications necessary to perform the functions of a Medical Physicist as well as other professionals in this vast field. The author suggests that one of the ways to accelerate and improve the installation of nuclear medicine services in Mozambique would be to create partnerships with national and international institutions such as the port's IPO, for example. However, before installing a Nuclear Medicine service, it is necessary to always maintain a continuous quality assurance program in accordance with international recommendations on the use of ionizing radiation for clinical purposes.

As for the examples of quality control in Nuclear Medicine, we were able to verify that in the case of linearity, the dosimeters used to measure activities are in the recommended range and ensure their effectiveness for clinical purposes. Regarding extrinsic and intrinsic uniformities, we found that their implementation varies from manufacturer to manufacturer, that is, the procedures and data analysis are different from each other. The developed software provides results within a tolerance of 7% for uniformity similar to ImageJ and Plugins. The sensitivity test suggests the need to improve the efficiency of the detectors in some cases, although the result obtained is within tolerance, we found that, for example, in the case of the Philips Brightview camera range, it has low sensitivity when compared to the most recent ones.

As future work, quality control and safety protocols in Nuclear Medicine for camera and PET equipment were improved, including more quality control tests in order to obtain recommendations that satisfy local problems that adapt to our reality. This developed program will be implemented in Mozambique, starting with the creation of a basic Nuclear Medicine service and followed by its practical implementation.

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# Attachments

## Code developed for data processing and analysis in Python

```python
def dicom_dataframe_generator(DICOM_folder_path):

    #É possivel extrair mais elementos da imagem adicionando nova column
    data_columns = ["Image ID"] + ["Gamma Camara ID"]+ ["Detector ID"] + ["Image Array"]

    data_rows = []

    for foldername, subfolders, filenames in os.walk(DICOM_folder_path):
        for filename in filenames:

            file_path = os.path.join(foldername, filename)
            data_set = dicom.read_file(file_path)
            image = data_set.pixel_array

            ###
            if len(data_set.DetectorInformationSequence) == 1:

                try:
                    det = data_set.ImageID
                except AttributeError:
                    det = data_set.SeriesDescription


                row = [filename] + [data_set.Manufacturer] + [det] + [image]
                data_rows.append(row)

            else:
                for i in range(image.shape[0]):

                    atrb1 = data_set.DetectorInformationSequence
                    atrb2 = atrb1[i].ViewCodeSequence
                    det_sub = atrb2[0].CodeMeaning
                    image_sub = image[i,:,:]

                    row = [filename] + [data_set.Manufacturer] + [det_sub] + [image_sub]
                    data_rows.append(row)
            ###

    dataframe = pd.DataFrame(data_rows[:], columns=data_columns)

    return dataframe
```

```python
DICOM_folder_path = r"C:\Users\amizi\Desktop\JP - Uniformidade Intrinseca\Amizito\24042024_E.cam_sala 4_unif extr\DICOM"
#DICOM_folder_path = "C:/Users/19jbp/Desktop/Uniformidade Intrinseca/DICOM"
df = dicom_dataframe_generator(DICOM_folder_path)

df
```

| | Image ID | Gamma Camara ID | Detector ID | Image Array |
|---|---|---|---|---|
| 0 | EE880E0C | SIEMENS NM | DET1 | [[0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,... |
| 1 | EE880E0C | SIEMENS NM | DET2 | [[0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,... |

```python
image_1=df["Image Array"][0]
image_2=df["Image Array"][1]


# image_1=cv2.resize(image_1, dsize=(128, 128))
# image_2=cv2.resize(image_2, dsize=(128, 128))

#plt.imshow(image_1, cmap=plt.cm.gray)
#print("image array dimensions:", image_1.shape)
#plt.imshow(image_2, cmap=plt.cm.gray)
#print("image array dimensions:", image_2.shape)


# Create subplots
fig, axes = plt.subplots(1, 2, figsize=(10, 5))

# Plot the first filtered image
axes[0].imshow(image_1, cmap='gray')
axes[0].set_title('image_1')
axes[0].axis('off')

#Plot the first filtered image
axes[1].imshow(image_2, cmap='gray')
axes[1].set_title('image_2')
axes[1].axis('off')
```

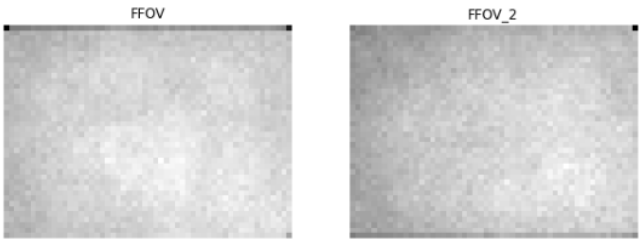
```
(-0.5, 63.5, 63.5, -0.5)
```

```
def FOV_array_generator (image_array):

    # Find the first and last non-zero rows and column

    non_zero_columns = np.where(~np.all(image_array == 0, axis=0))[0]
    distance_from_left = non_zero_columns[0]
    distance_from_right = image_array.shape[0] - non_zero_columns[-1] - 1
    if distance_from_left < distance_from_right:
        horizontal_margin_FFOV = distance_from_left + int(image_array.shape[0] * 0.025)
    else:
        horizontal_margin_FFOV = distance_from_right + int(image_array.shape[0] * 0.025)

    non_zero_rows = np.where(~np.all(image_array == 0, axis=1))[0]
    distance_from_top = non_zero_rows[0]
    distance_from_bottom = image_array.shape[1] - non_zero_rows[-1] - 1

    if distance_from_top < distance_from_bottom:
        vertical_margin_FFOV = distance_from_top + int(image_array.shape[1] * 0.025)
    else:
        vertical_margin_FFOV = distance_from_bottom + int(image_array.shape[1] * 0.025)


    # Crop the array symmetrically
    #FFOV -> Imagem da região do detetor (remover a borda de zeros)
    FFOV_array = image_array[vertical_margin_FFOV:-vertical_margin_FFOV, horizontal_margin_FFOV:-horizontal_margin_FFOV]

    #UFOV -> 95% da Areas do FFOV
    horizontal_margin_UFOV =  int(FFOV_array.shape[1] * (1-np.sqrt(0.95)) / 2)+1
    vertical_margin_UFOV =  int(FFOV_array.shape[0] * (1-np.sqrt(0.95)) / 2)+1

    UFOV_array = FFOV_array[vertical_margin_UFOV:-vertical_margin_UFOV, horizontal_margin_UFOV:-horizontal_margin_UFOV]

    #CFOV -> 75% da Areas do UFOV
    horizontal_margin_CFOV =  int(UFOV_array.shape[1] * (1-np.sqrt(0.75)) / 2)+1
    vertical_margin_CFOV =  int(UFOV_array.shape[0] * (1-np.sqrt(0.75)) / 2)+1

    CFOV_array = UFOV_array[vertical_margin_CFOV:-vertical_margin_CFOV, horizontal_margin_CFOV:-horizontal_margin_CFOV]

    return FFOV_array , UFOV_array, CFOV_array
```

```
FOVs = FOV_array_generator(image_1)
FOV_s= FOV_array_generator(image_2)

FFOV = FOVs[0]
UFOV = FOVs[1]
CFOV = FOVs[2]

FFOV_2 = FOV_s[0]
UFOV_2 = FOV_s[1]
CFOV_2 = FOV_s[2]
```

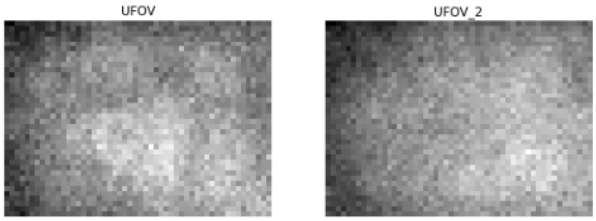
```
#plt.imshow(FFOV, cmap=plt.cm.gray)
#print("image array dimensions:", FFOV.shape)


# Create subplots
fig, axes = plt.subplots(1, 2, figsize=(10, 5))

# Plot the first filtered image
axes[0].imshow(FFOV, cmap='gray')
axes[0].set_title('FFOV')
axes[0].axis('off')

#Plot the first filtered image
axes[1].imshow(FFOV_2, cmap='gray')
axes[1].set_title('FFOV_2')
axes[1].axis('off')
```

```
(-0.5, 53.5, 39.5, -0.5)
```

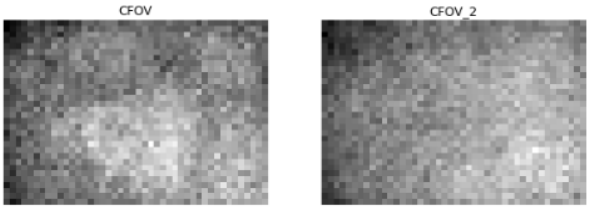


```
#plt.imshow(UFOV, cmap=plt.cm.gray)
#print("image array dimensions:", UFOV.shape)


# Create subplots
fig, axes = plt.subplots(1, 2, figsize=(10, 5))

# Plot the first filtered image
axes[0].imshow(UFOV, cmap='gray')
axes[0].set_title('UFOV')
axes[0].axis('off')

#Plot the first filtered image
axes[1].imshow(UFOV_2, cmap='gray')
axes[1].set_title('UFOV_2')
axes[1].axis('off')
```

```
(-0.5, 51.5, 37.5, -0.5)
```

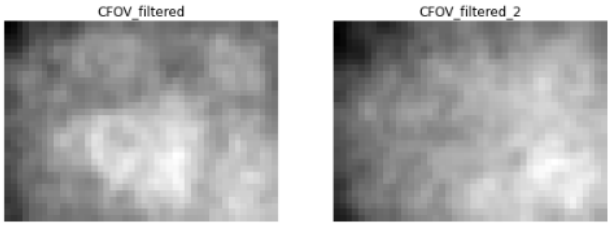



```
#plt.imshow(CFOV, cmap=plt.cm.gray)
#print("image array dimensions:", CFOV.shape)

# Create subplots
fig, axes = plt.subplots(1, 2, figsize=(10, 5))

# Plot the first filtered image
axes[0].imshow(CFOV, cmap='gray')
axes[0].set_title('CFOV')
axes[0].axis('off')

#Plot the first filtered image
axes[1].imshow(CFOV_2, cmap='gray')
axes[1].set_title('CFOV_2')
axes[1].axis('off')
```




```
### Noção do que está a ser realizado na aplicação de um filtro à imagem
### Na ferramenta computacional envez da função filter_applyer usou-se
### cv2.filter2D()

def filter_applyer(image_array,filter_array,eliminate_border_bool=False):

    # Apply the filter using convolution (filtered image with 0 borders)
    filtered_image_array = np.zeros_like(image_array)

    for i in range(1, filtered_image_array.shape[0] - 1):
        for j in range(1, filtered_image_array.shape[1] - 1):
            filtered_image_array[i, j] = np.sum(image_array[i-1:i+2, j-1:j+2] * filter_array)

    if eliminate_border_bool:
         # Eliminate border lines and columns
        filtered_image_array = filtered_image_array[1:-1, 1:-1]

    return filtered_image_array
```

```
filter_3x3 = np.array([[1, 2, 1],
                       [2, 4, 2],
                       [1, 2, 1]])

filter_3x3_norm = filter_3x3/filter_3x3.sum()

FFOV_filtered = cv2.filter2D(FFOV,-1,filter_3x3_norm)
UFOV_filtered = cv2.filter2D(UFOV,-1,filter_3x3_norm)
CFOV_filtered = cv2.filter2D(CFOV,-1,filter_3x3_norm)


FFOV_filtered_2 = cv2.filter2D(FFOV_2,-1,filter_3x3_norm)
UFOV_filtered_2 = cv2.filter2D(UFOV_2,-1,filter_3x3_norm)
CFOV_filtered_2= cv2.filter2D(CFOV_2,-1,filter_3x3_norm)
```




]:
```python
def UI_calculator(image_array):
    max_int = np.max(image_array)
    min_int = np.min(image_array)
    UI_int = (max_int - min_int)/(max_int + min_int)*100

    UI_dif = {}
    UI_dif['column'] = [0,(0,0)]
    UI_dif['row'] = [0,(0,0)]

    for i in range(2, image_array.shape[0]-2):
        for j in range(2, image_array.shape[1]-2):

            column_pixels = image_array[i-2:i+3, j]
            row_pixels = image_array[i, j-2:j+3]

            # Finding maximum and minimum values
            max_column = max(column_pixels)
            min_column = min(column_pixels)
            max_row = max(row_pixels)
            min_row = min(row_pixels)

            UI_dif_column = (max_column - min_column)/(max_column + min_column)*100
            if UI_dif_column > UI_dif['column'][0]:
                UI_dif['column'] = [UI_dif_column,(i,j)]

            UI_dif_row = (max_row - min_row)/(max_row + min_row)*100
            if UI_dif_row > UI_dif['row'][0]:
                UI_dif['row'] = [UI_dif_row,(i,j)]

    return (UI_int,UI_dif)
```