X Congreso Regional Latinoamericano IRPA de Protección y Seguridad Radiológica
"Radioprotección: Nuevos Desafíos para un Mundo en Evolución"
Buenos Aires, 12 al 17 de abril, 2015
SOCIEDAD ARGENTINA DE RADIOPROTECCIÓN

QUALITY CONTROL OF RADIOPHARMACEUTICAL DOSE CALIBRATORS IN NUCLEAR MEDICINE UNIT

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ABSTRACT

As part of the program to ensure quality in nuclear medicine unit, in addition to diagnostic procedures, are evaluated activity meters, which is intended to measure the aliquot of radiation of radionuclides and / or radiopharmaceuticals that are administered to patients undergoing diagnostic investigation and / or therapeutic treatment. The good operating condition of dose calibrators is essential to ensure efficiency, safety and reliability of the measurements, once the lack of accuracy in the responses of these equipments can cause significant errors in the activity administered to the patient and may result in poor quality images resulting in the repetition of examis and interference in the successful treatment of the patient. This study aims to, considering the need for constant evaluation of the functioning of the activity meters and the fact that this issue be part the responsibilities of the professional of radiology, perform quality control testing of these instruments in relation to the most recent norm of National Commission of nuclear Energy (CNEN-NN 3:05) in Brazil, that is also in according to the international standards and reference values established during acceptance testing of these instruments in a nuclear medicine service. For this, was made a review of specific literature and the use of barium, cobalt and cesium to the tests in a nuclear medicine service of the state of Pernambuco in Brazil. The obtained results of the specific tests utilized to verify the correct working of the dose calibrators show coherency with the resolutions of the CNEN-NN 3:05 and are also in agreement with the international standards to that the measurement of activities be made with accurate results and thereby contribute to the proper functioning of nuclear medicine service.

1. INTRODUCTION

The main feature of nuclear medicine image formation is that the radiation source is within the patient's body through a radionuclide together with drug substance which is an easier interaction with the organ to be studied, this being called junction radiopharmaceutical [Scott, 1999]. Thus, the image formation in nuclear medicine has its origin in part radioisotope administration, making it necessary to implement a Quality Control Program (QCP) for radioactivity measurements of these radiopharmaceuticals before being introduced into the patient. This implementation is crucial to the safe and effective use of these substances used in diagnostic and therapeutic procedures. [JUNIOR, A. C., 2006]

For measuring the activity of radiopharmaceuticals is used an instrument called a dose calibrator, curiometro or activimeter as it is better known. The activimeter is essential to ensure the efficiency and safety measures must always be in good working order. All

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radiopharmaceuticals are then subjected to the activity measurement by the instrument prior to administration to patients. If the instrument indicates a pH of less activity than the actual value, this will lead radiopharmaceutical administration with greater activity than the prescribed for the patient, without benefit of that extra dose; Thus, the patient is unnecessarily exposed. On the other hand, if the instrument indicate a value greater activity than the actual value, the administered activity will be insufficient for its intended purpose, resulting in repetition of the procedure, which, again, will lead to an unnecessary increase of the dose to patient and to occupationally exposed individuals involved. [DEBERTIN, K., 1992; Capintec 2001]

The National Commission of Nuclear Energy - CNEN establishes rules from the safety requirements and radiation protection for nuclear medicine services, recommended quality control tests in radiation measuring instruments, and qualified professionals to carry out these tests , ensuring the minimization of risks and maximizing the benefits of the use of ionizing radiation. These standards are updated as needed and new technologies are being developed to respect the use of ionizing radiation sources. In December 2013, the standard 3.05 proposes new requirements for ensuring the satisfactory performance of activímetros used in a nuclear medicine service, which also comes in line with international requirements for such purposes and which must be performed [CNEN-NN 3.05 , 2013; IAEA, 2000].

New activimeters shall be subjected to quality control to the acceptance of the instrument in the service that will be used, while the used appliances must do so periodically as the frequency defined by the standard 3.05 of CNEN in Brazil, which is the latest for these purposes.

2. LITERATURE REVIEW

2.1. An activimeter and its operation

An activimeter is a well-type ionization camera within which one places a sample to be measured.

It consists primarily of:

1. Ionization chamber,
2. source of high voltage stabilized,
3. electrometer for very low ionisation current measurements,
4. electronic Microprocessor (for calculation of activity) and
5. Digital display.

The ionization chamber is sealed filled with air or other suitable gas under some pressure. The radiation source produces ion pairs, i.e., a molecule with a positive charge and a negatively charged electron. If a voltage between the electrodes is not applied, the ion pairs recombine quickly. However, if a high voltage is applied between the electrodes, the positively charged molecule will be directed to the outer electrode while the electron will be directed to the collector electrode, so that there is a small electrical current between the electrodes. [ALVAREZ, 2004; NPL, 2006]

In general, the high voltage applied to the ionization chambers for use in activímetros is between 100 and 400 volts, because it must be high enough to collect most of the pairs of ions, but low enough to avoid causing ions produced other ionization as they are directed to the electrodes [CIEMAT, 2003].

The amount of ionization produced, or the amount of electric current is directly proportional to the activity of the radionuclide. The current is converted into voltage and amplified by an electrometer, which generally shows the voltage value in a digital display in units of activity [CIEMAT, 2003; IAEA, 1991].

Modern activímetros can be constructed with a microprocessor that calculates, for example, the volume required for a specific dose at a particular time of day. They can be coupled to a printer or computer for easy printing of labels and distributed doses records [A LOPEZ, 2005].

It is extremely important to perform quality control in activímetros because the accuracy of the dose of a radiopharmaceutical given to a patient depends on the operation of the activity meter. A series of quality control procedures are needed to ensure that the activímetro has a precise operation and reliable. The sources of 133Ba, 137Cs and 57Co are the most suitable for the implementation of quality control testing of the instrument, as they are sources with different energies, medium and low life activity in order of μCi.. [CIEMAT 2003].

With regard to quality control of activity meters are proposed by CNEN 8 tests are: repeatability; adjustment in zero; background radiation; high voltage; accuracy; precision; linearity; and geometry test [CNEN-NN 3:05, 2013] which also confirms the tests proposed by international standards related to quality control in activity meters [IAEA, 2000].

Was followed the instructions related to the equipment itself for completion of each test. For the high voltage, adjustment in zero and background radiation, just the touch of a button on the dose calibrator for it show its result and thus be made the assessment relating to the acceptable parameters set by the standard in question. In the test of repeatability, the sources are measured every day and are then investigated following a response pattern, or are offset with great fluctuations outside the acceptable by CNEN [CARPINTEC, 2001; CNEN-NN 3:05, 2013].

Generally, the ionization chamber is calibrated by the manufacturer using a set of sources screened to a national standardized laboratory. Commercial activímetros have a pre-selection for the most commonly used radionuclides, besides having the possibility of adjusting for other types. To the sources of Ba-133, Co-57 and Cs-137, an adjustment is carried out in equipment positioning the button intended for this regulation on channel 191, 112 and 220 respectively [BESSA, 2008].

The accuracy describes the degree of agreement between the result of a measurement and a true value of the activity; the precision describes the degree of agreement between the results of successive measurements of activity, carried out under the same conditions, and repeated in a short period of time. The linearity tests the long term stability of the activímetro. If the same measurement can be reproduced for several half-lives of a radioactive source, the instrument will be considered linear, indicating, for a particular radionuclide, the range where the radionuclide activity can be correctly estimated. When the original calibration set a dose calibrator, manufacturers generally use radionuclide solution in a given container. Other containers used in nuclear medicine units, such as plastic or glass syringes, and volumes can

have different absorption properties, and must be determined for these other correction factors consisting of the geometry test of these instruments. [BESSA, 2008; IAEA, 1991].

This paper aims to apply quality control tests in activímetro a nuclear medicine service located in Pernambuco, Brazil, according to the latest standard of CNEN, getting a diagnosis on the operating status of the activity meter.

3. METHODOLOGY

In this study,the quality control tests established by CNEN were performed in activimeter a nuclear medicine service located in the state of Pernambuco, Brazil.

The activímetro used for the application of the tests are shown in **Fig. 1.** model CRC-7 and serial number 71,885, manufactured by the Capintec, which has approximately 60% of activimeters in use in Brazil by nuclear medicine systems. [BESSA, 2008]

FIGURE 1: Activimeter model CRC-7 - Capintec. Photo kindly given by the Center of Nuclear Medicine of Pernambuco (CEMUPE) in Brazil.

The sources used for checking the quality of the activity meter were the indicated by CNEN for these purposes, which are the sources of barium-133 calibrated on 05/04/2013, cobalt-57 calibrated on 04.29.2013 and cesium-137 calibrated on 04/05/2013, respectively as shown in **Fig. 2**.

FIGURE 2: Sources A, B, and C corresponding to Ba-133, Co-57 and Cs-137, respectively, used as standards for quality control in activimeters. Photo kindly given by the Center of Nuclear Medicine of Pernambuco (CEMUPE) in Brazil.

For the application of the tests mentioned above in activímetro, were adopted procedures in accordance with national schemes developed for quality control of these devices [CNEN-NN 3:05, 2013], which also confirms the international protocols of radiological protection and safety in medicine nuclear [IAEA, 1991].

The first of four daily tests set to be held, was the **high voltage** test and then the **adjustment in zero,** the **background radiation** test and the r**epeatability.** Later, the semi-annual testing **accuracy** and **precision** were performed, respectively.

To perform the **high voltage** test, was activated the button on the machine where the response corresponded to power activímetro battery, which according to the manual of the equipment, must be between 140 and 155Volts [CARPINTEC, 2001]. As for the **adjustment in zero**, through the control panel is possible to adjust the value of the output signal voltage of the radiation detector to be very small (close to zero) or zero when the radiation in the environment is very low.
To obtain the value of the **background** radiation, the activity was measured without any source or radiopharmaceutical within the curiômetro and to complete the daily testing repeatability was made by measuring each source (Ba-133, Co-57 and Cs-137) three times to check the constancy of the machine's response, with the necessary adjustment corresponding to each radionuclide, positioning the channel in the range of 591, 112 and 220, respectively.

Later, the semi-annual testing **accuracy** and **precision** were performed by collecting 10 measures the activity of each source (Ba-133, Co-57 and Cs-137), subtracting the background radiation values after each measurement, and then performing the calculations for obtaining the results of each test. For accuracy, we used the calculation:
*E (%) = 100 * (1- Average of the activities measured / real activity). As for accuracy, made use of the calculation P (%) = (Average of activities measures individually) / Average of measures * 100.*

The **linearity** of the reference system response was tested by monitoring the radioactive decay of a sample of technetium-99m eluted in which the initial activity was 275 mCi, in a 6 ml solution in a vacuum glass jar produced by the Institute of Nuclear and Energy Research (IPEN). The appropriate operating conditions for technetium-99m have been selected. With the source in the well of the chamber, a measurement was obtained. The day and the measurement of time were recorded. This procedure was repeated each hour during a day.

The **Figure 3** shows the activity as a function of time elapsed from the first measurement and the theoretical curve based on the decay of the source calculated from measurements performed after beginning the test. No individual measurements diverged from activity acceptance limit recommended in the manufacturer's manual (± 10%), which indicates that the instrument response is linear over the activity range in which the test was performed.

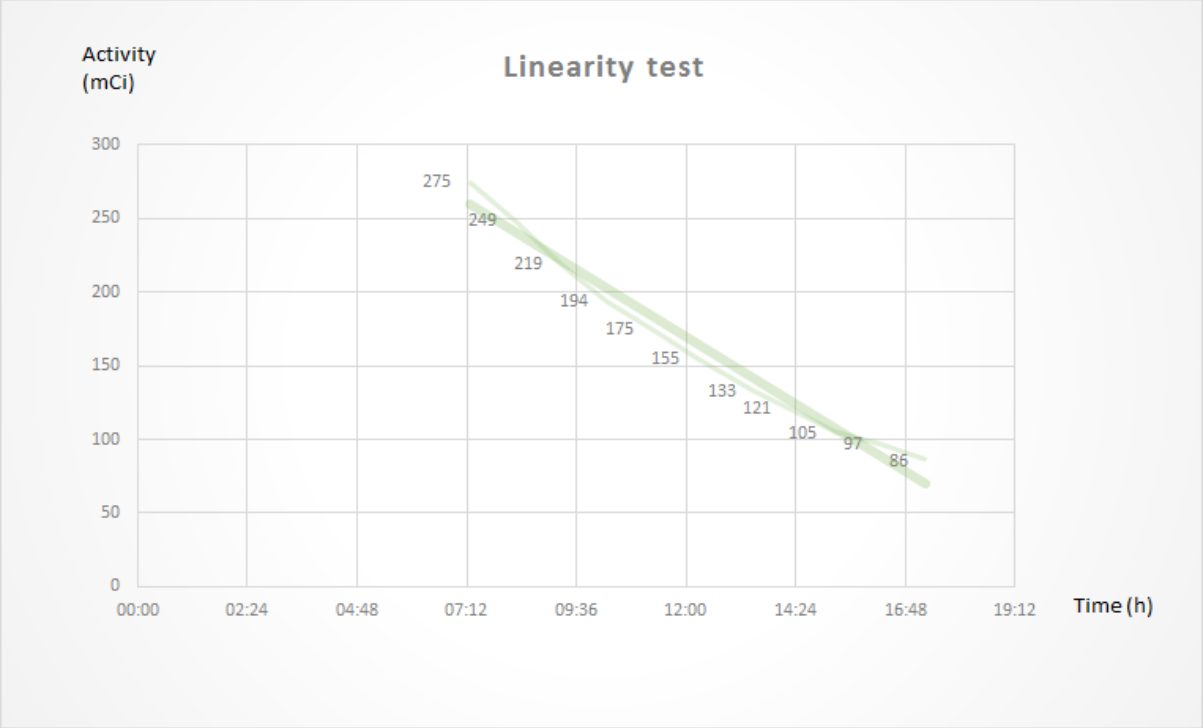

Figure 3: graph representing the activity measured in mCi versus time in hours estimated from measurements taken after the beginning of the linearity test.

In the **geometry** test was evaluated as the change in the activity depending on the volume of a sample, keeping the amount of radioactive material present (99m) in the reference dose calibrator.

Plastic disposable syringes of 3 ml , 5 mL and 10 mL was used in an initial sample volume of 0.5 ml. The sample volume in the syringes was gradually increased with adding distilled water, 0.5 and 0.5 ml up to reach the maximum volume of each syringe. After each addition, was stirred gently syringe to become homogeneous radioactive solution. When the maximum volume of each syringe was reached, its content was transferred to a vacuum glass jar produced by the Institute of Energy and Nuclear Research (IPEN) and a new measurement of the sample was taken. Then were determined correction factors, dividing the activity measured in glass jar vacuum by the activities measured in the syringe.

From the results obtained, there were assessments of the state of activimeter.

2. RESULTS AND DISCUSSION

According to the results, the constancy observed in the equipment with respect to the high-voltage and zero-setting tests, the results being 0 and 151 volts respectively, which comes into agreement with the acceptable parameters provided by the manual own instrument, the national standard CNEN-NN 3:05 updated in 2013 and also by the international standard [IAEA, 1991], which guides the voltage of activímetro have a maximum variance in the response ± 1% should be between 140 and 155 Volts, and the zero-setting is very close to zero or zero.

With regard to background radiation tests, there was wide variation in results, with a maximum deviation of 87.7% and the minimum deviation of 2.85%, lying often beyond the standard indicated by 3:05 CNEN which suggests that this deviation is at maximum ± 20%. However, the justification is given by the time and the actual test, which varied according to need and availability of equipment, and is often performed after measurements of radiopharmaceuticals activity and possible contamination.

In the teste of repeatability, the values achieved, although they are not listed, are within acceptable parameters by the rules in question and the measures to be within a range of ± 5%.

In the accuracy tests, the results were 1% deviation for the Ba-133, 4.126% for Co-57 and 2.4% for Cs-137, with the values obtained by the three sources within the range indicated by CNEN which is ± 10%.

In the test accuracy, the values obtained were 3.76% for Ba-133, 1.28% for Co-57 and 3.01% for Cs-137, all of them within the CNEN range which is indicated by ± 5%.

The **Fig 3.** shows equipment response linearity with respect to the sample activity of technetium-99, which obtained results according to the parameters set by CNEN and others international standards with regard to quality control of activity meters.

The geometry test allowed the observation of the variation of activímetro response with the source volume at a concentration of constant activity, with an average correction factor using a 3 ml syringe 0.967, 0.939 for the use of 5 ml syringe and 0.973 when using the 10ml syringe.

The results obtained show that the activímeter is getting a good performance, because it showed excellent levels of accuracy and precision by 3 sources of reference, response linearity and response variation with the source volume at a concentration of constant activity, in which the results are shown within the acceptable limits, indicating the high quality metrology of this system, in addition to high voltage testing, zero-setting and repeatability are also within the parameters indicated by the standard CNEN 3.05 and international regulations related with the control of quality in activimeters.

3. CONCLUSION

In order to obtain a good performance of a nuclear medicine service, the activimeter used must be within the required operating parameters so that there is a great potential of response of the radiopharmaceuticals activity that will be injected into the patient and thus, get pictures examination with good quality to enable an accurate diagnosis, collaborating with the health and safety of the patient and individuals occupationally exposed to radiation. Activities such as the quality's control tests of these instruments are extremely important to check if the activimeter is or is not providing reliable information of the activities it measures. These activities are related to radiology's technologist and therefore, it was a great opportunity for radiology course student effectively develop their skills and also allowed to obtain a diagnosis on the operation status of a activimeter in a nuclear medicine unit in Pernambuco in

Brazil, which according to the results achieved, showed compliance with the recommendations of the CNEN and also of international organizations related to the assessments performed.

4. REFERENCES

1. A LÓPEZ, L.A.; TORRES, M. A.; COCA, G. L., eds. Protocolo Nacional para el Control de Calidad de Instrumentos de Medicina Nuclear. CIEN, 2005.
2. ALVAREZ, O. T. B.; CALDAS, L. V. E.. **Controle de qualidade em câmara de ionização tipo poço usada em braquiterapia de baixa taxa de dose**. In: Anais do IX Congresso Brasileiro de Física Médica, Rio de Janeiro. 2004, v. CD-ROM. p. 1-4. Comissão Nacional de Energia Nuclear 2004.
3. BESSA, A. C. M.; COSTA, A. M.; CALDAS, L. V. E. **Levantamento do controle de qualidade de calibradores de dose de radiofármacos em serviços de medicina nuclear na cidade de São Paulo.** Radiol. Bras. v. 51, p. 115-118, 2008.
4. CAPINTEC. **Radioisotope dose calibrator**, CRC 15 BT Owner's manual, 2001.
5. CIEMAT "PCA: Protocolo para la calibración y el uso de activímetros". Documento de consenso entre la Sociedad Española de Medicina Nuclear, Sociedad Española de Física Médica, Laboratorio de Metrología de Radiaciones Ionizantes del CIEMAT, Sociedad Española de Protección Radiológica, Radiofarmacia, 2003.
6. COMISSÃO NACIONAL DE ENERGIA NUCLEAR. **Requisitos de Radioproteção e Segurança para Serviços de Medicina Nuclear. Rio de Janeiro**: CNEN, 2013. (CNEN-NE-3.05).
7. DEBERTIN, K.; SCHRÄDER, H. **Intercomparisons for quality assurance of activity measurements with radionuclide calibrators**. Nucl. Inst. Meth. Phys. Res., A312, p. 241-245, 1992.
8. INTERNATIONAL ATOMIC ENERGY AGENCY. **Quality control of nuclear medicine instruments**. Vienna, 1991. (IAEA-TECDOC-602).
9. INTERNATIONAL ATOMIC ENERGY AGENCY. **Handling, conditioning and storage of spent sealed radioactive sources**. Vienna: IAEA, 2000. (IAEA-TECDOC-1145).
10. JUNIOR, A. C.; **Introdução à Radiologia**. Ed. Rideel, cap. 7, p. 71-72, 2006.
11. NATIONAL PHYSICAL LABORATORY - NPL. **Protocol for establishing and maintaining the calibration of medical radionuclide calibrators and their quality control**. Measurement Good Practice Guide No. 93. UK, 2006.
12. SCHRADER, H. **Activity measurements with ionization chambers**, BUREAU INTERNATIONAL DES POIDS ET MESURES. Monographie BIPM-4, 1997.
13. SCOTT, A. M. The state of the art in nuclear medicine. In: The Third Conference on Nuclear Science and Engineering in Australia. A nuclear renaissance. Australia, 1999. p. 71-73.