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CONSTANCY TESTS AND QUALITY ASSURANCE OF THE ACTIVIMETERS USED IN A RADIOPHARMACEUTICAL PRODUCTION UNIT

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ABSTRACT

Activimeters (or dose calibrators) are essential instruments to verify activity of radiopharmaceutical after production and also before the dose administration in humans or animals for molecular imaging. The efficiency and safety measurements depend on, beside other factors, constancy tests and quality assurance. Thereby, the aim of this work was to perform constancy tests and quality assurance in the activimeters of the UPPR/CDTN, based on the CNEN-NN 3.05 Brazilian standard and the manufacturer's manual. Physical inspection, auto zero, background check, camera voltage, data check and constancy test were done. In addition, accuracy and precision tests were performed using a set of standard certified radioactive sources (^{57}Co, ^{133}Ba and ^{137}Cs), according to the CNEN NN 3.05 Brazilian standard. Linearity test was also performed to evaluate the response of the equipment in over the entire range of activities used in routine. The equipments are periodically submitted to the quality control tests and the results were compared. After performing the proposed tests it is possible to conclude that activimeters are in accordance with the requirements of the CNEN standard and manufacturer´s manual. A quality control checklist was prepared to guide users and to record the results of quality assurance testing to monitor the equipment performance. This initiative is part of the quality assurance program implemented at UPPR.

1. INTRODUCTION

The Radiopharmaceuticals Research and Production Unit (UPPR) at the Nuclear Technology Development Center of National Nuclear Energy Commission (CDTN/CNEN) produce traditional and new radiopharmaceuticals in a cyclotron facility for positron emission tomography (PET) use. A small animal scanner is used in pre-clinical studies for the development of new radiopharmaceuticals or in new applications of traditional radiopharmaceuticals.

The radionuclides used in research activities at UPPR have short half-lives and are not sealed sources, which means that the injection of properly measured doses is one of the guarantee

that small animals will not obtained an inconclusive imaging result or receive a radioactive dose beyond what is really necessary.

In this context, activimeters (or dose calibrators) are essential instruments in radiopharmacy to verify the activity of the radiopharmaceutical after production and also before the dose administration in the animal for molecular imaging.

This instrument had to be used by trained professionals and had the quality control performed frequently, which is essential to guarantee the measurements reliability [1, 2, 3].

The aim of this work was to perform constancy tests and quality assurance in the activimeters of the UPPR/CDTN, based on the CNEN-NN 3.05 Brazilian standard [4] and the manufacturer's manual [5].

2. MATERIALS AND METHODS

All experiments were carried out at the Radiopharmaceutical Research and Production Unit (UPPR/CDTN/CNEN).

2.1. Equipment description

In this study two similar activimeters were used (CRC®-25R, Capintec, Inc) and consists basically of one display unit (readout), the well type ionization chamber and respective dipper device. (Fig. 1) [5].

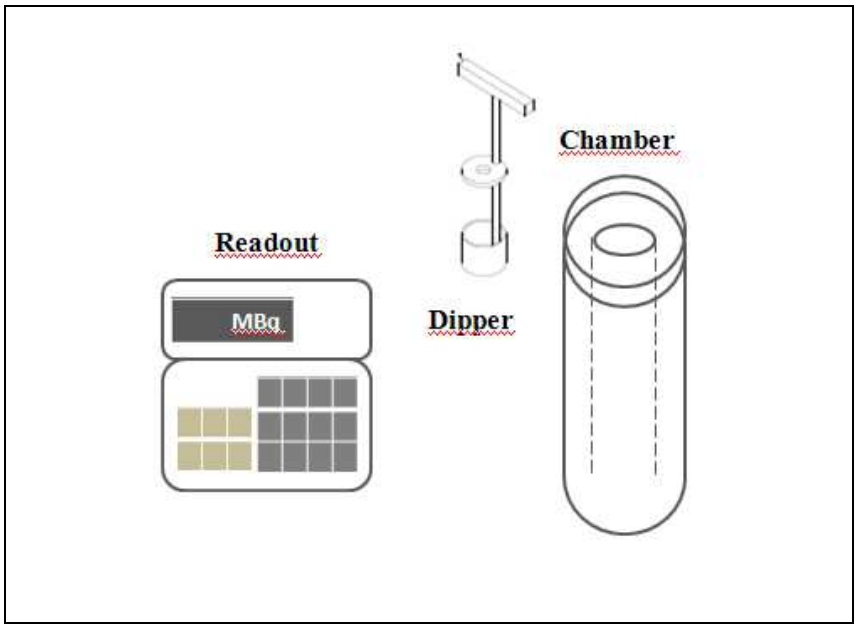


Figure 1: Schematic view of activimeter device.

Table 1 contains the main features about the activimeters used in this work.

Table 1: Activimeters features used [5]

Manufacturer / Model	Gas Chamber	Height Chamber (cm)	Diameter Chamber (cm)	Maximum Activity (^{57}Co)	Resolution
CAPINTEC / CRC®-25R	Argon	43.8	17.2	206 GBq (5.57 Ci)	0,001 MBq (0,01 µCi)

2.2. Standard Sources

The three standard recommended sources by CNEN NN 3.05 are ^{57}Co, ^{133}Ba and ^{137}Cs (Fig. 2). All have a long half-life and similar energy range to the gamma energy emitted by radionuclides produced and/or used in experimental routine. Table 2 presents the main physical-chemical features about the radioactive sources. All sources were provided by Nuclear and Energy Research Institute (IPEN/CNEN), however ^{133}Ba and ^{137}Cs have NIST traceability certificates and ^{57}Co is under the agreement EA MLA.

Figure 2: Sealed reference sources for quality control of the activimeter.
Note: Left to right: ^{57}Co; ^{133}Ba; ^{137}Cs.
Source: UPPR/CDTN Gallery, 2017

Table 2: Main features about radionuclides used

Radionuclide	Main photon energy (keV)*	Half-Life*	Certified Activity (MBq)	Reference Date
^{57}Co	122.06065 ± 0.00012	271.74 d	201 ± 5	1st August 2016
^{133}Ba	356.0129 ± 0.0007	10.551 y	9.687 ± 0.031	09 December 2016
^{137}Cs	661.657 ± 0.003	30.08 y	6.209 ± 0.016	30 September 2016

*** Source:** IAEA Live Chart of Nuclides, 2017 [6].

2.3. Experiments

Physical inspection, auto zero, background check, camera voltage, data check and constancy test were done. In addition, accuracy and precision tests were performed. A set of standard certified radioactive sources (^{57}Co, ^{133}Ba and ^{137}Cs) were used, according to the Brazilian standard. The linearity was checked over the entire range of activities commonly used in daily routine at the UPPR. Linearity test was performed using decay method of measuring a short lived isotope (^{18}F) over time.

All tests were done based on the information obtained in the CNEN NN 3.05 standard and the manufacturer's manual (Table 3).

Table 3: Periodicity of the main quality control tests according to the protocol consulted.

Tests	Frequency of Tests	
	CNEN NN 3.05 [4]	**Manufacturer Manual [5]**
AutoZero	Daily	Daily
Background	Daily	Daily
Voltage Chamber	Daily	Daily
Data Check (^{57}Co; ^{133}Ba; ^{137}Cs)	Daily	Daily
Accuracy	Semiannually	Daily
Precision	Semiannually	Daily
Linearity	Annually	For improvement (No recommended period)

The results of both instruments for daily, semiannually and annually tests were compiled and are presented in next section. The data set comprises one year of tests: from 2016 to 2017.

In addition, environmental conditions like temperature and air relative humidity were accompanied during the period of tests. The equipment manufacturer establishes environmental conditions limits: the instruments should be located where the temperature is stable within a range (+10 °C to +30 °C) and the maximum relative humidity is 90 % [5].

3. RESULTS AND DISCUSSIONS

In this section, the results for physical inspection, daily tests (auto zero, background check, camera voltage, data check and constancy), and also accuracy, precision and linearity tests are presented.

First of all, temperature varied between 18.1 °C and 23.1 °C. The air relative humidity was always between 34 % and 46 %. The environment conditions observed are within limits established by manufacturer over the period evaluated.

3.1. Physical Inspection and Daily Tests

Both equipments were intact in physical verification, without any structural damage. All devices and reading display worked properly.

In the all daily tests for both activimeters throughout evaluated period (applied voltage in the camera, background radiation, zero adjustment and data check) the message "OK" to continue, was showed on the display, which indicates that they are working properly.

The results of Auto Zero, background and chamber voltage checks for both activimeters are shown in Fig. 3, 4 and 5, respectively.

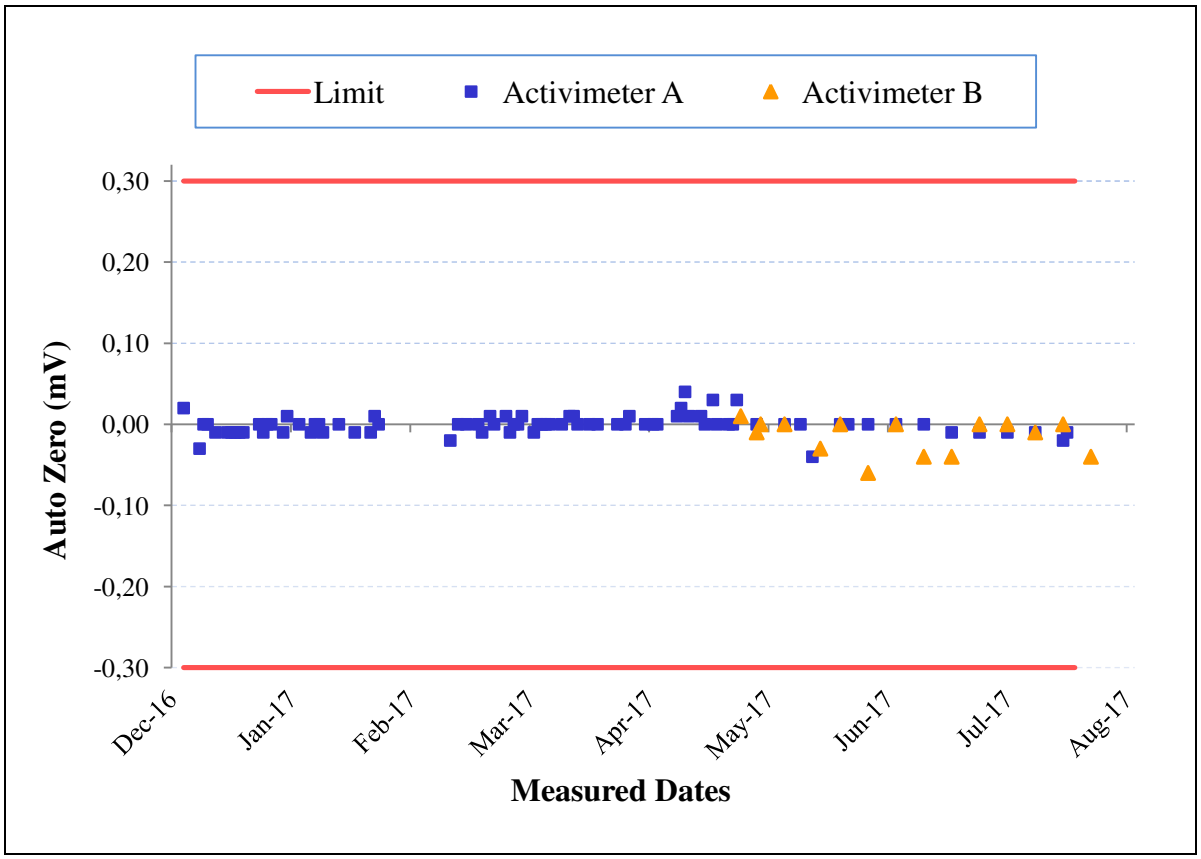
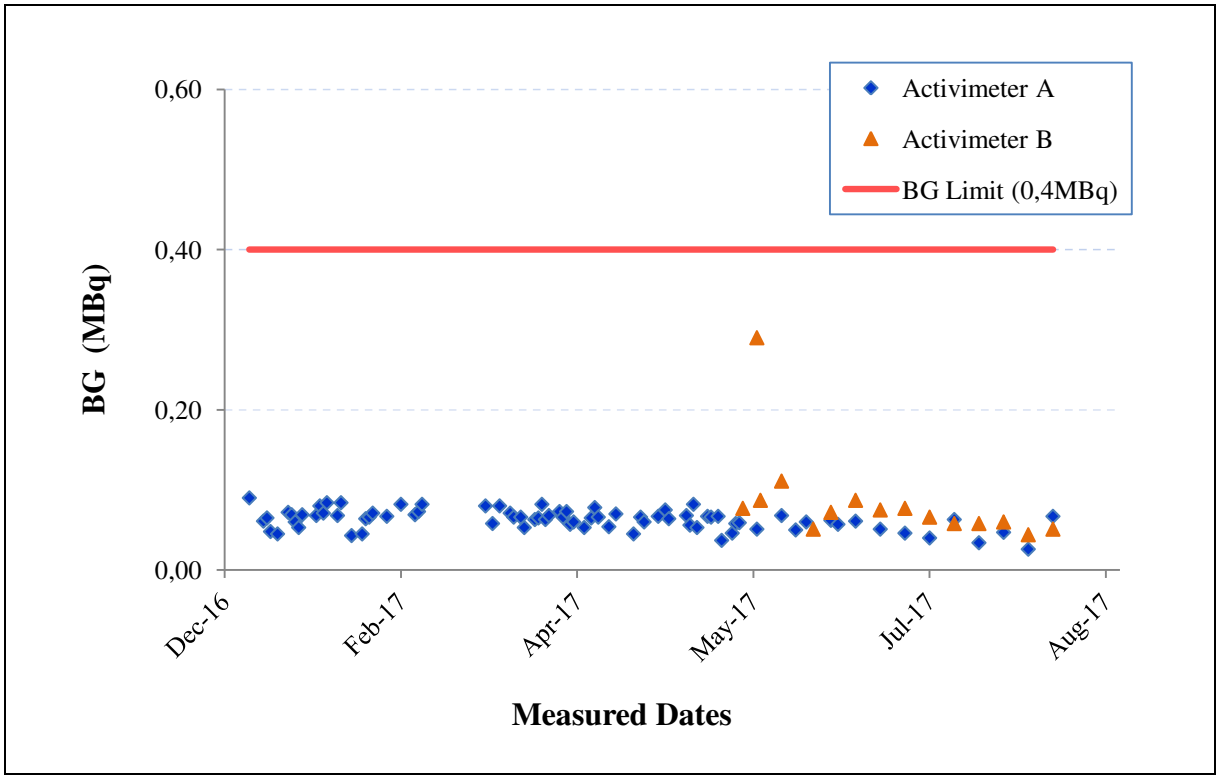


Figure 3: Auto Zero check results for both activimeters.
(Upper and lower limits are established by manufacturer).



Figures 4: Background check results for both activimeters. (Upper and lower limits are established by manufacturer).

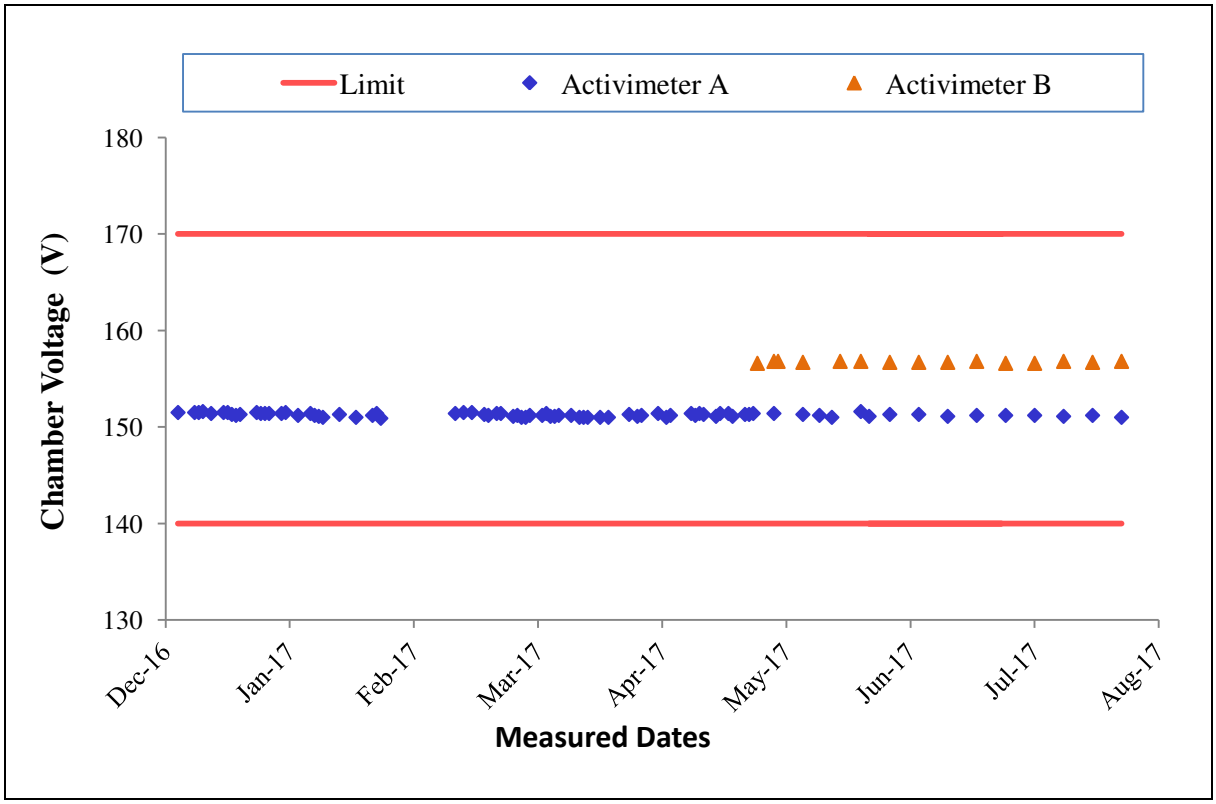


Figure 5: Chamber Voltage check results for both activimeters. (Upper and lower limits are established by manufacturer).

3.2. Repeatability Test

Fig. 6, 7 and 8 present results for both activimeters used based on known reference sources (^{57}Co, ^{133}Ba and ^{137}Cs, respectively).

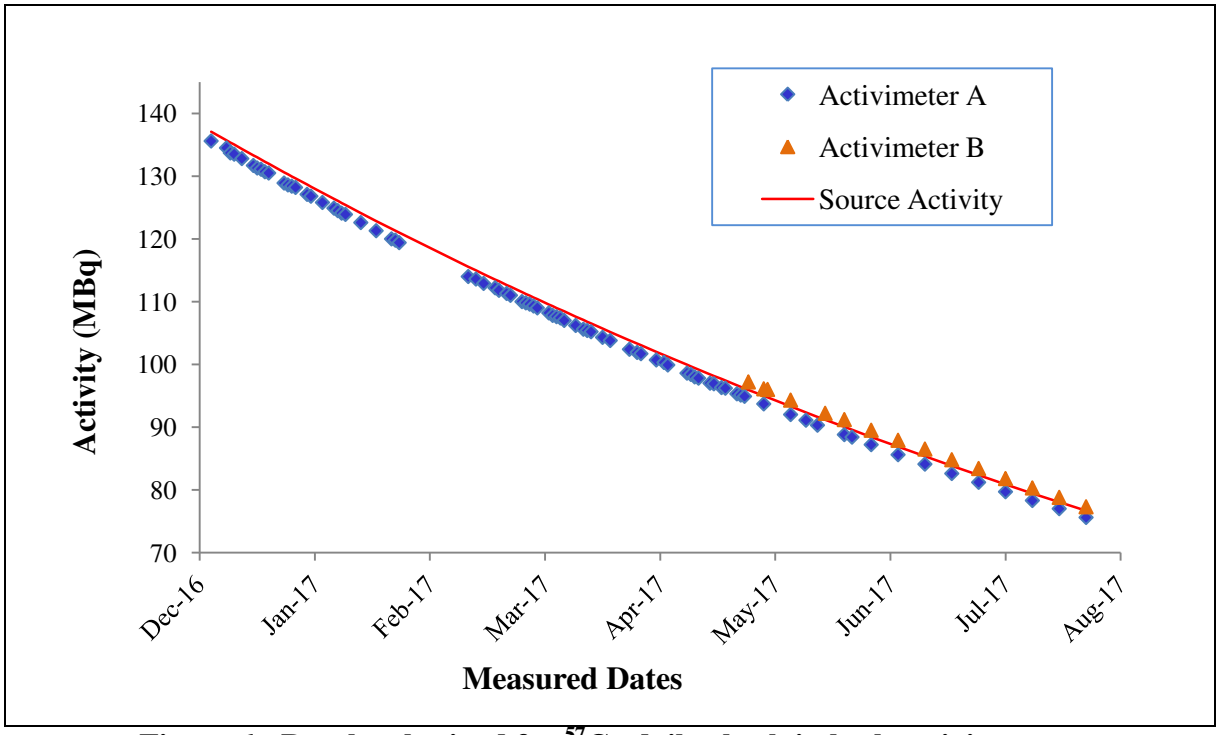


Figure 6: Results obtained for ^{57}Co daily check in both activimeters. The red line indicates the source activity calculated from the certified activity.

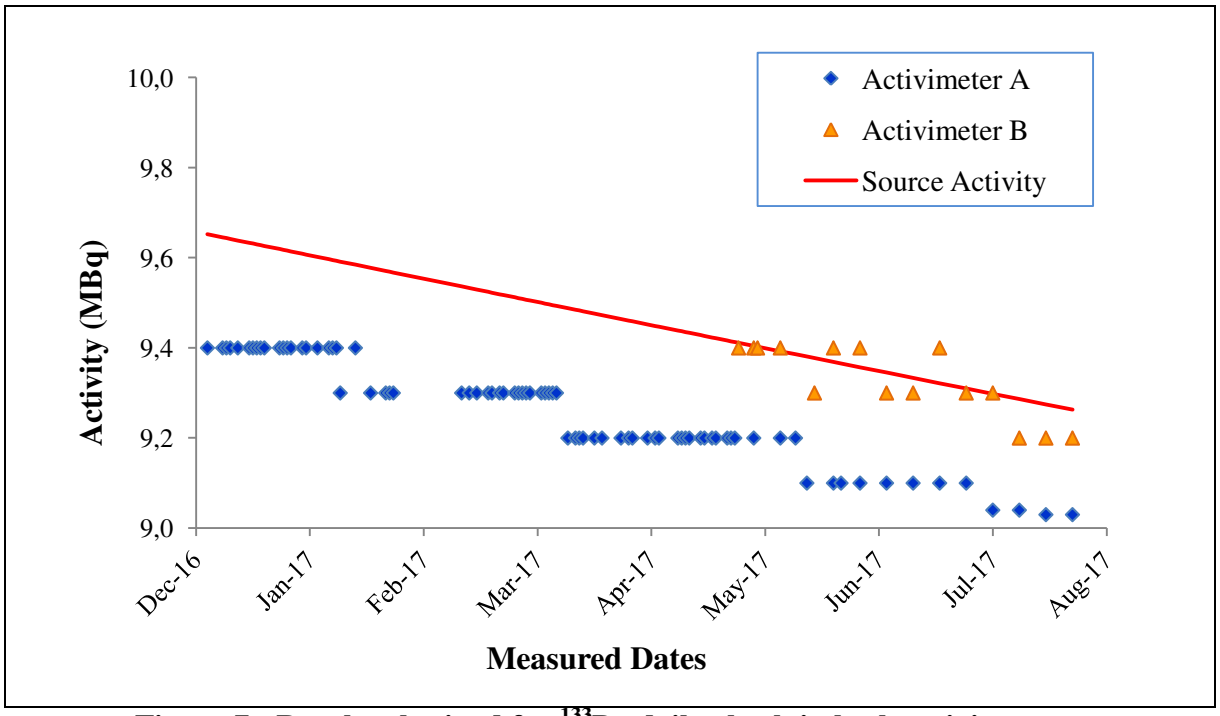


Figure 7: Results obtained for ^{133}Ba daily check in both activimeters. The red line indicates the source activity calculated from the certified activity.

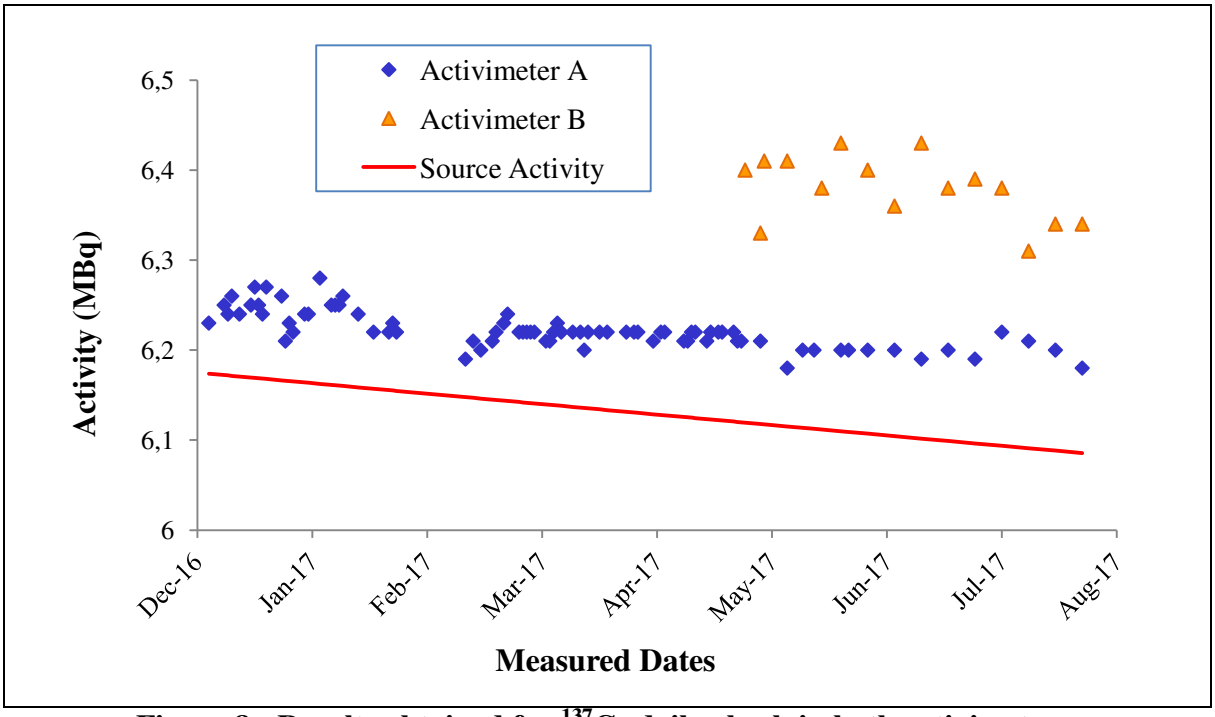


Figure 8: Results obtained for ^{137}Cs daily check in both activimeters. The red line indicates the source activity calculated from the certified activity.

The purpose of the test is to check the operation constancy of a device over time, for different measurement conditions. The measurements should be within a range of ± 5 % [4].

Although the equipments shows different results, all activity values from reference sources obtained in activimeters A and B are within the limits recommended by national and international standards.

3.3. Accuracy and Precision Tests

Table 4 shows results for accuracy and precision measurements in relative standard deviation (RSD) for both instruments.

Table 4: Results obtained for accuracy and precision test in both activimeters.

Tests	Relative Standard Deviation of Activity (RSD)			
	First Semester		Second Semester	
	Activimeter A	Activimeter B	Activimeter A	Activimeter B
Accuracy	- 1.40	---	- 1.41	- 3.94
Precision	0.21	---	0.20	0.18

The measurements should be within a range of ± 10% for Accuracy and ± 5% for Precision [4].

3.4. Linearity test

Fig. 9 presents results of the linearity test for the activimeter A.

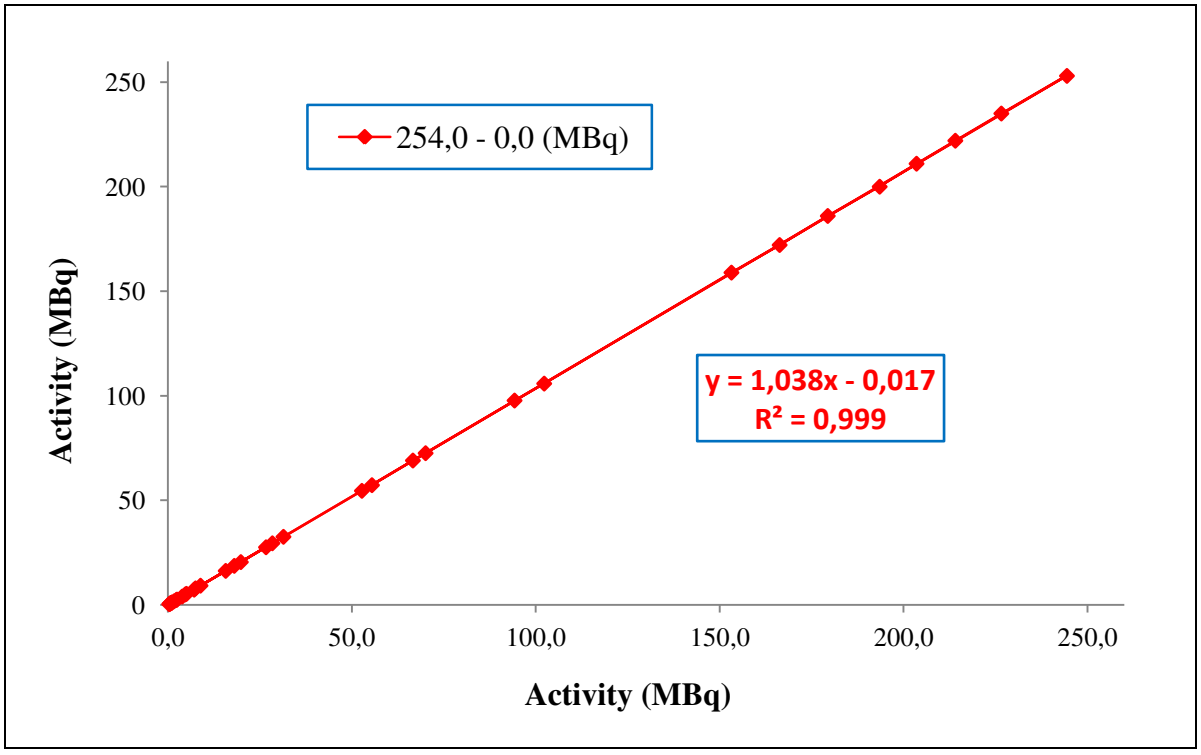


Figure 9: Linearity result for activimeter A.

The linearity test should be within a range of ± 10% [4]. The results show a linear behavior in a large range of activity (0.29 to 250 MBq) for the tested activimeter.

4. CONCLUSIONS

The study demonstrated that after the stabilization time recommended (30 minutes) by the manufacturer, the system obtained reliable measurements. No damage was found in the visual inspection.

The obtained results indicate that the UPPR's activimeters are stable over period evaluated. All values are inside the limits presented in the manufacturer´s manual and national standard for all tests done. This stability is of paramount importance for the reliability of all processes involved in molecular imaging.

In addition, a quality control checklist was prepared to guide users and record the results of quality assurance testing to monitor the equipment performance. This initiative is part of the quality assurance program implemented at UPPR.

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