Survey on quality control of radiopharmaceutical dose calibrators in nuclear medicine units in the city of São Paulo, SP, Brazil*

Levantamento do controle de qualidade de calibradores de dose de radiofármacos em serviços de medicina nuclear na cidade de São Paulo

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Abstract **OBJECTIVE: To perform a survey on routine quality control tests of dose calibrators at nuclear medicine units in the city of São Paulo, SP, Brazil. To evaluate the accuracy of measurements of seven dose calibrators activities, utilizing sources of clinically significant radionuclides at the calibration laboratory of Instituto de Pesquisas Energéticas e Nucleares. MATERIALS AND METHODS: The survey on quality control of dose calibrators has been based on questionnaires answered by the nuclear medicine units. Seven dose calibrators, Ga-67, Tc-99m and Tl-201 sources and a secondary standard instrument have been utilized in the accuracy study. RESULTS: The survey results on the quality control tests of the dose calibrators showed some inappropriateness, for example, the absence of daily reproducibility tests in all of the units. The accuracy tests for the seven dose calibrators showed results within the acceptable limit in compliance with the national regulations (± 10%). CONCLUSION: According to the few nuclear medicine units participating in the survey, the dose calibrators quality control is unsatisfactory. The accuracy study of seven dose calibrators has not demonstrated any performance faults, and has established the calibration of these instruments for the utilized sources.**

Keywords: Nuclear medicine; Dose calibrators; Calibration; Quality control.

Resumo **OBJETIVO: Realizar levantamento sobre quais testes de controle de qualidade são realizados nos calibradores de dose dos serviços de medicina nuclear da cidade de São Paulo, SP. Estudar a exatidão das medições de atividade de sete calibradores de dose no Laboratório de Calibração de Instrumentos do Instituto de Pesquisas Energéticas e Nucleares, usando fontes de radionuclídeos importantes clinicamente. MATERIAIS E MÉTODOS: O levantamento sobre o controle de qualidade foi realizado a partir de questionários enviados aos serviços. Foram utilizados, no estudo de exatidão dos sete calibradores de dose, fontes de Ga-67, Tc-99m e Tl-201 e um instrumento padrão secundário. RESULTADOS: Os resultados do levantamento sobre os testes de controle de qualidade mostraram algumas impropriedades, por exemplo, a falta da realização diária do teste de reprodutibilidade por todos os serviços. Os resultados do teste de exatidão para os sete calibradores de dose estudados mostraram-se dentro do limite de aceitação da norma nacional (± 10%). CONCLUSÃO: A situação com relação ao controle de qualidade de calibradores de dose é insatisfatória, de acordo com o pequeno número de serviços que participaram do levantamento. O estudo da exatidão em sete calibradores de dose não indicou falhas de desempenho e estabeleceu uma calibração desses instrumentos para as fontes utilizadas.**

Unitermos: Medicina nuclear; Calibradores de dose; Calibração; Controle de qualidade.

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INTRODUCTION

A dose calibrator is an essential device in a nuclear medicine unit, utilized for determining the activity of radiopharmaceuticals (pharmaceuticals labeled with radionuclides) administered to patients both for diagnostic and therapeutic purposes. Essentially, it consists of a well-type ionization chamber coupled with a special electronic circuit which allows the display of the instrument response in activity units. Should the instrument indicate an activity value lower than the actual value, the patient will be given a radiopharmaceutical with a higher-than-prescribed activity; being unnecessarily exposed to extra radiation. On the other hand, should the instrument indicate an activity value higher than the actual value, the administered activity will be insufficient, requiring repetition of the procedure and also implying an unnecessary increase in dose to the patient and

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to occupationally exposed individuals involved in the process.

Aiming at assuring a satisfactory performance of the dose calibrator utilized in a nuclear medicine unit, the Comissão Nacional de Energia Nuclear (CNEN) — National Commission of Nuclear Energy — determines that these instruments are semestrally submitted to accuracy, precision and linearity tests, and daily to reproducibility tests[1]. Although CNEN does not require geometry testing, it is recommended that this test is performed at dose calibrators installation[2–5].

On activity measurements, accuracy describes the degree of agreement between a measurement result and an actual activity value; precision describes the degree of agreement between results of successive activity measurements performed under identical conditions, and repeated at short time intervals. Reproducibility tests are related to long term dose calibrators stability. If a same measurement can be reproduced over a period of several half-lives of a radioactive source, the instrument response will be rated as linear, indicating, for a particular radionuclide, the range where the radionuclide activity can be correctly estimates (linearity). Dose calibrators manufacturers usually utilize radionuclide solutions in a determined container to define the original calibration of the device. Other containers utilized in nuclear medicine units, such as plastic or glass syringes may present different volumes and absorption properties, so other correction factors should be determined for such containers, consisting in geometry testing of the instruments.

Usually, commercial dose calibrators are originally calibrated by manufacturers with standard radionuclide solutions (direct calibration) of a national or traceable standards laboratory, or, alternatively, by comparison with a reference instrument (indirect calibration). In this type of calibration (indirect), a comparison between the reading of the instrument to be calibrated and the reading of the directly calibrated reference instrument is made by introducing a reference source under identical conditions for measurement in each ionization chamber well. Operational conditions of the source to be measured are applied, and the reading of the first instrument is adjusted, or a correction factor is obtained.

The calibration or recalibration of a dose calibrator may be based on the accuracy tests with clinically significant radionuclide sources. Currently, the standard CNEN-NN-3.05[1] requires only accuracy tests with reference ^{57}Co, ^{133}Ba or ^{137}Cs sources, and not with clinically significant radionuclide sources. Those three sources cover the range of utilization of a dose calibrator, and are assigned to simulate the geometry of a short-half-life radionuclide solution in a similar container. The ^{57}Co source simulates a ^{99m}Tc source, the ^{133}Ba source simulates a ^{131}I source, and the ^{137}Cs source simulates a ^{99}Mo source. Should a dose calibrator accuracy is tested with a ^{57}Co source, for example, the appropriate operational condition is selected for ^{57}Co and not for ^{99m}Tc. As a result, the instrument is not tested for the portion of its electronic circuit dedicated to the measurement of ^{99m}Tc activity. Generally, this shortcoming is observed for all of the clinically significant radionuclide sources. Therefore, significant errors may arise from activity measurements utilizing operational conditions of dose calibrators which are not directly tested for accuracy.

This instruments calibration or recalibration also may be undertaken by means of intercomparison. Studies published in the period between 2003 and 2005[6–10] demonstrate the increasing necessity of implementing a program of quality control for dose calibrators in nuclear medicine units.

So, a survey on quality control tests and their respective frequency was undertaken in nuclear medicine units in the city of São Paulo. A preliminary survey on the accuracy of activity measurements in dose calibrators also was undertaken with seven devices, utilizing clinically significant radionuclide sources in the Laboratório de Calibração de Instrumentos (LCI) (Calibration Laboratory) of Instituto de Pesquisas Energéticas e Nucleares (IPEN).

MATERIALS AND METHODS

Initially, a survey on dose calibrators existing in the city of São Paulo was undertaken. This survey was based on a questionnaire sent with a form to 87 nuclear medicine units. Later, a second questionnaire with questions regarding dose calibrators quality control were sent to those unities which had answered the first questionnaire.

A survey on the accuracy of activity measurements performed with dose calibrators was undertaken with seven instruments called A, B, C, D, E, F and G, in the LCI-IPEN. These dose calibrators are described on Chart 1. These dose calibrators accuracy was tested for ^{67}Ga, ^{99m}Tc and ^{201}Tl sources. These clinically utilized radionuclide sources were provided by the IPEN Centro de Radiofarmácia in cylindrical, flat-bottomed, colorless glass flasks with 47.0 mm in height, 23.5 mm external diameter, and wall thickness of 1.1 mm. These are the IPEN standard flasks for radiopharmaceuticals supply. The samples volume was 4 ml.

The accuracy of dose calibrators was indirectly checked, utilizing a reference instrument. The readings of the instrument under test and of the reference instrument were compared by means of a same source under identical measurement conditions in each ionization chamber well. The percentage deviation between the average of activities measured on the instrument under test and the average of activities measured on the reference instrument was utilized for determining the accuracy of the tested instrument. The accuracy test acceptance limit recommended by the standard CNEN-NN-3.05[1] is ± 10%.

The NPL-CRC dose calibrator (Southern Scientific Ltd.), of the LCI-IPEN, was utilized as reference system. This dose calibrator was calibrated by the primary standard laboratory in England — National Physical Laboratory — and therefore it is a secondary standard system.

Chart 1 Dose calibrators utilized in the accuracy study.

Manufacturer	Model	Quantity	Designation
Capintec	CRC®-15R	4	A, B, C e D
Capintec	CRC®-35R	2	E e F
Victoreen	34-056 Deluxe II	1	G

RESULTS

Among 87 nuclear medicine units included in the survey on dose calibrators in the city of São Paulo, only 22 filled in and returned the forms about 26 calibrators. No type of response or communication was received from the other 65 units contacted. The results are shown on Chart 2.

Among the 22 nuclear medicine units which had returned the firs form/questionnaire, only eight filled in and returned the second form/questionnaire with questions about dose calibrators quality control. No type of response or communication was received from the other 14 units. Among the eight nuclear medicine units which had returned the form, three reported the unavailability of reference standard sources for quality control tests; one of them utilizing reference standard sources borrowed from other nuclear medicine units to perform quality control tests, one performed only a semestral linearity test, and one did not perform any test. The frequency of quality control tests in these nuclear medicine units is shown on Tables 1 to 4.

The results of the survey on accuracy of activity measurements performed with seven dose calibrators in the LCI-IPEN, utilizing ^{67}Ga, ^{99m}Tc and ^{201}Tl as reference sources are shown on Table 5. In all of the measurements, the percentage deviation between the average of activities measured on the instrument under test and the average of activities measured on the reference instrument was < 5%.

As already mentioned, the calibration of a dose calibrator may be based on an accuracy test. Table 6 presents the ratios between the values of the measured activities of the reference instrument and those of the instrument under test. Uncertainties were not assigned to these values, considering that type B uncertainties[11] in measurements with the reference dose calibrator were not estimated. These values determine correction factors, that is to say, numeric factors by which the non-corrected results are to be multiplied to balance systematic errors, establishing a calibration (or recalibration) of the dose calibrators tested for the radionuclides utilized.

DISCUSSION

There are 26 dose calibrators in the 22 nuclear medicine units which filled in and returned the form/questionnaire on dose calibrators existing in the city of São Paulo (Chart 2). About 58% of these dose calibrators are manufactured by Capintec.

Table 1 demonstrates that only one of the eight nuclear medicine units which filled in and returned the second forms/questionnaires with questions related to dose calibrators quality control, had performed the geometry test at the device installation, and three had never performed such test; in only one of the units the accuracy test is semestrally performed, and in four this test is more frequently performed (Table 2). Among the tests required by the standards CNEN-NN-3.05[1], the reproduc-

Chart 2 Types of dose calibrators existing in nuclear medicine units of São Paulo.

Manufacturer	Model	Quantity
Alfanuclear	CD-50	1
Capintec	CRC®-7	5
	CRC®-10	1
	CRC®-10BC	1
	CRC®-12R	1
	CRC®-15R	7
Siemens	Curietest	1
Veccsa	Vexcal	3
Victoreen	34-056 Deluxe II	3
	34-061 CAL/RAD Digital*	3

* Geiger-Müller tubes – well configuration.

Table 1 Frequency of geometry tests in eight nuclear medicine units of São Paulo.

Frequency	Number of units
Only at installation	1
Daily	1
Quartely	1
Semestrally	1
Yearly	0
Never	3
Other	1

Table 2 Frequency of accuracy tests in eight nuclear medicine units of São Paulo.

Frequency	Number of units
Only at installation	0
Daily	1
Quartely	3
Semestrally	1
Yearly	0
Never	1
Other	2

Table 3 Frequency of reproducibility tests in eight nuclear medicine units of São Paulo.

Frequency	Number of units
Only at installation	0
Daily	0
Quartely	2
Semestrally	1
Yearly	0
Never	3
Other	2

Table 4 Frequency of linearity tests in eight nuclear medicine units of São Paulo.

Frequency	Number of units
Only at installation	0
Daily	0
Quartely	3
Semestrally	3
Yearly	0
Never	1
Other	1

Table 5 Accuracy test: percentage deviation between the average of activities measured on the instrument under test and the average of activities measured on the reference instrument for ^{67}Ga, ^{99m}Tc e ^{201}Tl sources.

Dose calibrator	^{67}Ga	^{99m}Tc	^{201}Tl
A	+ 3.8	+ 4.0	+ 4.8
B	+ 2.3	+ 2.7	+ 3.0
C	+ 3.4	+ 3.7	+ 4.1
D	+ 3.4	+ 4.0	+ 3.8
E	+ 3.0	+ 3.5	+ 3.5
F	+ 3.6	+ 4.0	+ 3.8
G	+ 4.0	+ 2.7	+ 3.6

Table 6 Ratios between activity values measured on the reference instrument (A_v) and activity values measured on the instrument under test (A_m) for ^{67}Ga, ^{99m}Tc e ^{201}Tl sources.

Dose calibrator	A_v/A_m		
	^{67}Ga	^{99m}Tc	^{201}Tl
A	1.039	1.042	1.051
B	1.024	1.028	1.031
C	1.035	1.038	1.043
D	1.035	1.042	1.040
E	1.031	1.036	1.036
F	1.038	1.042	1.042
G	1.042	1.028	1.028

ibility test is the less frequently performed, as shown on Table 3. Reproducibility tests are particularly significant for evaluating the equipment operation constancy over the time for different measurements conditions. Linearity test is semestrally performed in three nuclear medicine units, and quarterly in three (Table 4).

Tables 1 to 4 results show some inappropriatenesses, for example, daily geometry tests in one unit (Table 1) and lack of daily reproducibility tests in all of the nuclear medicine units (Table 3). Maybe this is due to the lack of technical and bibliographic support for users of dose calibrators in nuclear medicine units in Brazil. The lack of technical support is a result from the distance between manufacturers and users, considering that this type of instrument is not manufactured in Brazil. On the other hand, the lack of bibliographic support could be solved with the cooperation of specialists from several institutions of the country, developing a publication including detailed information on quality control tests, defining the most appropriate format for data recording and presentation as well as tests frequency, following the example of other countries like Spain, with the study developed by Aguado et al.[4], and England, with the study developed by Gadd et al.[5].

Results included in Table 5 demonstrate that all of the tested dose calibrators meet the acceptance criteria (± 10%) defined by the standard CNEN-NN-3.05 for accuracy tests.

Mean values of the ratios between the activities measured on the reference instrument and activites measured on the instrument under test, calculated as per Table 6 are 1.035 ± 0.06, 1.037 ± 0.06 and 1.039 ± 0.08, respectively for ^{67}Ga, ^{99m}Tc e ^{201}Tl sources. Based on these values, one may be observe that there is trend to underestimate the values of activities measured for ^{67}Ga, ^{99m}Tc e ^{201}Tl sources. This trend has also been observed in other studies developed in Brazil[7].

CONCLUSIONS

Approximately 75% of nuclear medicine units in the city of São Paulo have not answered the first questionnaire about the types of existing equipment. Sixty-four percent of the nuclear medicine units which had answered the first questionnaire, did not answered the second one with questions related to dose calibrators quality control. Considering that no step was taken to minimize the lack of responses, the conclusions of the present study were limited by the size of the sampling. Notwithstanding, it may be concluded that the current situation of dose calibrators quality control in Brazil is unsatisfactory.

Accuracy tests were performed with seven dose calibrators for radionuclide sources with clinical purposes. This accuracy survey has not indicated any performance faults, and has established the calibration of these instruments for the utilized sources. Dose calibrators must be calibrated with clinically utilized radionuclide sources, although this is not required by the standard CNEN-NN-3.05[1]. This procedure can be undertaken by the LCI-IPEN.

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