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Proficiency test for radioactivity measurements in nuclear medicine

A. Iwahara · L. Tauhata · A. E. Oliveira · I. G. Nícoli · F. G. Alabarse · A. M. Xavier · M. L. Oliveira · M. F. Koskinas · M. C. M. Almeida

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Abstract Proficiency tests established by ISO/IEC-43 were applied to assess the performance of 69 Brazilian nuclear medicine services in the radiopharmaceuticals activity measurements of ^{131}I, ^{99}Tc^{m}, ^{67}Ga and ^{201}Tl. The 214 datasets originated from comparison programs promoted by the Laboratório Nacional de Metrologia das Radiações Ionizantes (LNMRI) in 2006/2007 were also evaluated against acceptance criteria of ±10% limits for accuracy required by Brazilian regulatory authority. The results of performance evaluation were assigned as "*Acceptable*" or "*Not-acceptable*" accordingly and have shown a large dispersion when the statistical criteria assays were applied and also compared with regulatory requirements.

Keywords Nuclear medicine · Proficiency test · Radionuclide calibrator · Radioactivity

A. Iwahara (✉) · L. Tauhata · A. E. Oliveira · M. C. M. Almeida
Instituto de Radioproteção e Dosimetria (IRD), National Nuclear Energy Commission, Av. Salvador Allende, s/n, Jacarepaguá, CEP 22780-160, Rio de Janeiro, RJ, Brazil
e-mail: iwahara@ird.gov.br

I. G. Nícoli
Escritório de Brasília (ESBRA), National Nuclear Energy Commission, SCN, Quadra 4, Bloco B, Sala 1002-B, Ed. VARIG—Asa Norte, CEP 70714-900, Brasília, DF, Brazil

F. G. Alabarse · A. M. Xavier
Distrito de Porto Alegre (DIPOA), National Nuclear Energy Commission, Av. Bento Gonçalves, 9500, Prédio 43.322—ILEA, CEP 91501-970, Porto Alegre, RS, Brazil

M. L. Oliveira
Centro Regional de Ciências Nucleares do Nordeste (CRCN-NE), National Nuclear Energy Commission, Av. Prof. Luiz Freire, 200, Cidade Universitária, CEP 50740-540, Recife, PE, Brazil

M. F. Koskinas
Instituto de Pesquisas Energéticas e Nucleares (IPEN/CNEN-SP), Avenida Professor Lineu Prestes, 2242, Cidade Universitária, CEP 05508-000, São Paulo, SP, Brazil

Introduction

The field of metrology of radioactivity is an important feature of life sciences activities. Due to the recognition of the implementation of Quality Assurance programmes to guarantee the consistency of the measurements it is easy to understand their application in the nuclear medicine practices [1–3]. The availability of standards with metrological traceability to calibrate instruments and to verify the performance of activity measurements enables the establishment of a quality control programme in the use of radiopharmaceutical products. In nuclear medicine services (NMSs), many types of radioactive substances are used for diagnostic and therapy routines. The equipment used to measure the activity is the radionuclide activity calibrator. This instrument is composed of an ionization chamber (or Geiger–Müller detector) coupled to an electrometer with a direct display reading in activity units.

The procedures related to activity measurements in NMSs are regulated by norms or requirements established by authorities that details the legal responsibilities in these fields. These regulations apply to the radiopharmaceutical suppliers, to the radionuclide calibrator manufacturers and to the users in NMSs. The regulations need to specify the necessary accuracy in the measurement of the activity of radiopharmaceutical products administered to the patient and the data must be available to the regulatory authority audits at any time. The International Atomic Energy

Agency [4] and European Pharmacopoeia [5] recommend a maximum deviation of ±5% when it refers to accuracy of measurement in radionuclide calibrators. In Brazil, the required accuracy for diagnostic purposes is established in the norm NN 3.05 of the National Nuclear Energy Commission (CNEN) [6] that requires percentage deviations up to ±10%.

The activity administered to the patient should be as close as possible to that prescribed by the physician. If it is smaller, the patient may probably need an additional administration to obtain the desired clinical result (for example, good image for diagnosis) and this results in an unwanted dose. If the activity is larger, the patient will equally be receiving an unnecessary dose. In both cases one of the basic principles of the radiation protection to the patient, the optimization, has been infringed.

To evaluate the performance of the quality of routine in the NMSs, LNMRI has been coordinating comparison programmes of activity measurements of radiopharmaceutical products used in nuclear medicine practices. Brazil is a large country having continental dimensions and NMSs are operating in all over the country mostly settled in the Southeast region. Because of this and the problem concerning the short half-life radionuclides involved it is impracticable sending the sample to another region from the main laboratory LNMRI localized at Rio de Janeiro state. To overcome these problems, regional laboratories have been implemented in diverse sites of the national territory establishing the National Metrology Network [7]. These laboratories own radionuclide calibrators traceable to the LNMRI and carry out comparison exercises with NMSs located in its region (Fig. 1).

In 2006/2007, a comparison exercise was organized with 69 NMSs participants distributed by geographical regions of Brazil (Table 1), involving the radionuclides $^{99}Tc^{m}$, ^{131}I, ^{67}Ga and ^{201}Tl. In this work, the requirements of IAEA [4] and ISO/IEC-43 [8] were applied with the purpose of homogenizing the evaluation procedure of the comparisons. The performance evaluation was also accomplished using the value of the ratio of the mean value of five measurements carried out by the participant NMSs and the value obtained by LNMRI adopted as the reference value to be compared with the normative requirement of Brazilian regulatory authority [6]. In this case the acceptance criterion is $0.9 \leq R \leq 1.1$.

Table 1 Distribution of NMSs participants by major regions of Brazil

Region	Number of NMS		
	Participants	Total	Participation (%)
North	0	4	0
Northeast	6	31	19
Southeast	41	152	27
South	12	40	30
Central West	10	20	50
Total	69	247	28

The two evaluation procedures looked at the accuracy of the results and the proficiency test consider also the precision including the total combined uncertainty associated with the measurement of the participant NMS as well as the uncertainty associated with the reference value.

Experimental

The proficiency test performance evaluation was applied to the results of each radionuclide. For each radionuclide, the

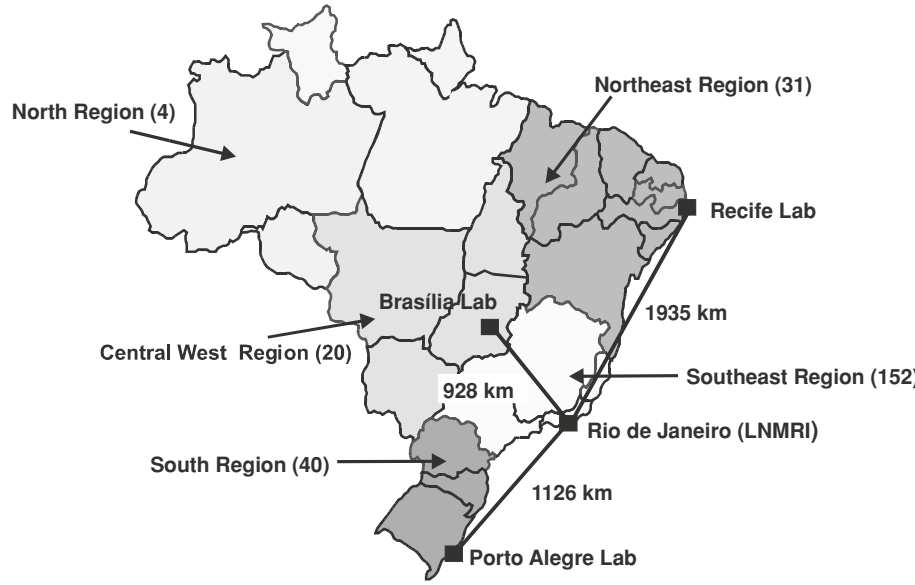

Fig. 1 The National Metrology Network of Radionuclides for comparisons of activity measurements in nuclear medicine services in Brazil. Number within brackets represents number of NMSs in each major region

reference value and its associated uncertainty were established by LNMRI using an IG12 ionization chamber that was calibrated with standard sources that, in turn, were standardized using the primary standardization systems set up at LNMRI.

In order to the overall NMS results to be assigned as "*Acceptable*", all of the individual criteria (with the exception of the Ratio Value) have to be "*Acceptable*". The final result of the performance evaluation was defined by the combined results of *Accuracy*, *Precision*, *Relative bias* and Z_{Score} according to the criteria established by ISO/IEC 43 [8]. Using this approach, the evaluation was applied to 214 results obtained in the comparison runs of radionuclide activity measurements of radiopharmaceutical products realized in 2006/2007.

Results and discussion

Before analyzing the performance, a statistical test [9] was applied to the collected data in order to identify and remove those data called *outliers* considering a normal distribution. In this way 13 results have been removed and 201 were analyzed as described in Table 2. The criterion accuracy indicated by U_{Score} values, calculated with $k = 1.96$, showed 55.2% of results to be "*Acceptable*" values, as shown in Fig. 2. This result is inconsistent with the value of 78.6% "*Acceptable*" values of *Relative bias*, but consistent with the value of 70.6% when we calculate U_{Score} with $k = 3$, for 99.7% confidence level. In this criterion, deviations greater than ±10% indicate that the value of activity obtained by an NMS was "*Not-acceptable*" or not conform, according to the requirement of Norm CNEN NN 3.05. These results indicate that the many NMSs need to optimize its activity measurement procedure. The evaluation for *Precision* criterion showed 100% of results to be "*Acceptable*" values, with all the results having values of less than 5%, indicating a good repeatability of the measurements.

The histogram of the frequency distribution of Z_{Score} values is shown in Fig. 3, with 97% of "*Acceptable*" results. The distribution behaved as a Gaussian and to illustrate this, a linear fitting was adjusted to the data where the goodness of fit is sustained by the correlation coefficient value $r^2 = 0.9837$ (Fig. 4). This data distribution showed an underestimation trend of the NMS mean value relating to the reference value.

The ratio values that classify the performance according to the criterion of Brazilian regulatory authorities are equivalents to the relative bias values with the same percentage of A*cceptable* values of 78.6%. A more detailed

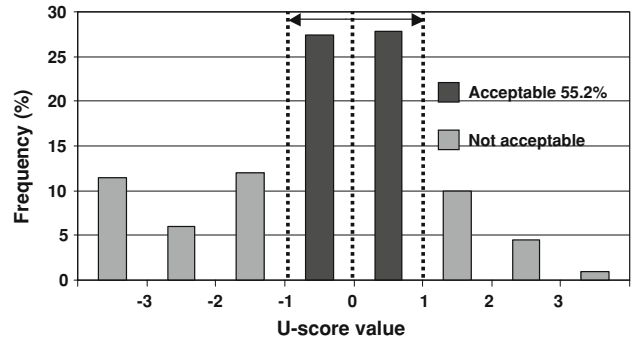

Fig. 2 Frequency distribution of U_{Score} values

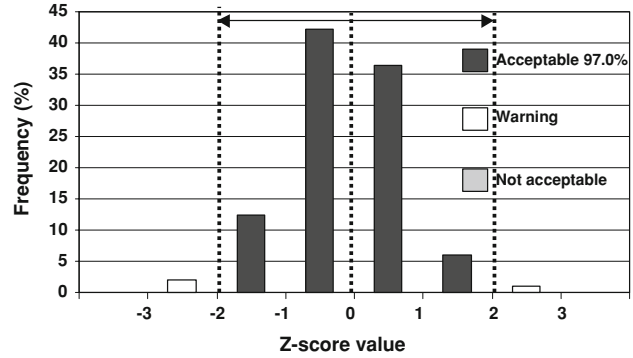

Fig. 3 Frequency distribution of Z_{Score} values

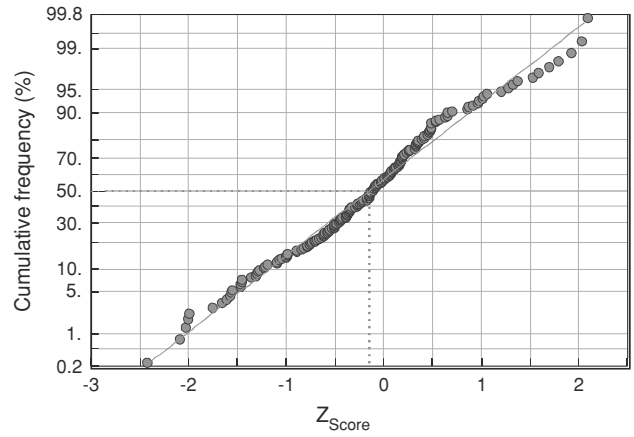

Fig. 4 Least square fitting of the Z_{Score} cumulative frequency distribution of 201 comparison data

Table 2 Collected and analyzed data for performance test of the comparison

Radionuclide	Collected data	Removed data	Analyzed data
^{67}Ga	47	3	44
^{201}Tl	40	2	38
^{131}I	68	6	62
^{99}Tc^{m}	59	2	57
Total	214	13	201

Table 3 Comparative performance of activity measurement for each kind of radionuclide in the radiopharmaceutical products, in the comparison runs realized in the period 2006/2007

Radionuclide	Number of measurements	Ratio [7] ($Value_{NMS}$/$Value_{LNMRI}$) $0.9 \leq R \leq 1.1$ (%)	Proficiency Test with 5% of precision [5] (%)
^{67}Ga	47	76.7	50.0
^{131}I	68	77.4	47.5
$^{99}Tc^{m}$	59	86.0	68.4
^{201}Tl	40	73.7	52.6
Total	214		

breakdown for the collected data with the fraction of acceptable values obtained in the comparison runs is shown in Table 3 for each radionuclide. For each radionuclide the acceptance performance required by the criteria of ISO 43 is much more restrictive than the regulatory requirement.

Radionuclide calibrators with Geiger–Müller detectors represent 24.9% of the total of instruments in the comparisons. Using the value of *Ratio* ($Value_{NMS}/Value_{LNMRI}$) to evaluate the performance of radionuclide calibrators provided with Geiger–Müller detectors, we note that only 60% of results were classified as "*Acceptable*". This result indicates that this kind of detector have a low performance for routine measurement of activity of the radiopharmaceutical products by NMSs. On the other hand, the performance of radionuclide calibrators provided with ionization chambers, 75.1% of the total of instruments, reaches the value of 84.8%.

Finally, the use of the combined statistical criteria of the proficiency tests shows that the 214 datasets of activity measurements of radionuclides in radiopharmaceutical products obtained in the comparison programmes with 69 NMS participants, have reached the value of 55.2% with the status "*Acceptable.*" This result indicates that the measurement of activity by NMSs needs to be improved in order to meet the requirements of the national norm and international recommendations. If we use a coverage factor of $k = 3$ in the calculation of U_{Score}, we obtain a value of 70.6% with the status "*Acceptable*". This result is similar as 78.6% established by the Brazilian regulatory requirement for Nuclear Medicine radioactivity measurements.

Conclusions

The poor performance of 55.2% for "*Acceptable*" results shows that NMSs need to improve their quality control in the measurement of activity in order to meet the requirements of good practices in the nuclear medicine and radiation protection fields. Nevertheless, if only the requirement of regulatory authority is taken into account a performance of 78.6% is attained. This shows that the ISO 43 performance evaluation criteria is much more restrictive providing more "*Not-acceptable*" performances than the *Ratio* criterion of Brazilian Regulation. Another conclusion is that those radionuclide calibrators that use Geiger–Müller detectors presented poor performance only reaching 60% of "*Acceptable"* results. These calibrators need to be replaced with those using ionization chambers that reaching 84.8% of "*Acceptable*" results. These comparison exercises also establish traceability in activity measurements of nuclear medicine practices in the country and may be used to take correcting and preventive actions to improve the quality of services afforded to the patients.

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