Proficiency test for radioactivity measurements in nuclear medicine*

Teste de proficiência para medições de radioatividade na medicina nuclear

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Abstract **OBJECTIVE: To assess the performance of radionuclide calibrators in 55 Brazilian nuclear medicine services in the measurement of $^{99}Tc^{m}$ radiopharmaceutical activity. Proficiency tests were applied to data sets with 63 results originated from the comparison program developed by Laboratório Nacional de Metrologia das Radiações Ionizantes of Instituto de Radioproteção e Dosimetria. MATERIALS AND METHODS: The calibrators' performance was evaluated in compliance with the acceptance criterion of ± 10% accuracy required by the Brazilian standards and also the criteria established by the ISO/IEC Guide 43-1, and classified as either "acceptable" or "non-acceptable". The samples of $^{99}Tc^{m}$ utilized in the comparison were supplied by some of the participants and calibrated at Laboratório Nacional de Metrologia das Radiações Ionizantes for determining the activity reference value. RESULTS: The present study utilizing $^{99}Tc^{m}$ has shown that 82.5% of the calibrators were considered as acceptable according to the Brazilian standards, while by the criteria established by ISO/IEC 43-1, 81.0% were considered as acceptable. On the other hand, radionuclide calibrators with Geiger-Müller detectors presented unsatisfactory performance when compared with calibrators with ionization chambers. CONCLUSION: The performance evaluation based on the ISO/IEC 43-1 criteria, which are applied to analytical laboratories, in spite of being more restrictive, has demonstrated to be quite consistent with the accuracy criterion established by the Brazilian standard.**

Keywords: Proficiency test; Radionuclide calibrator; Nuclear medicine; $^{99}Tc^{m}$.

Resumo **OBJETIVO: Avaliar o desempenho dos calibradores de radionuclídeos de 55 serviços de medicina nuclear brasileiros em medição de atividade de radiofármaco contendo $^{99}Tc^{m}$. Testes de proficiência foram aplicados em 63 resultados originados do programa de comparação promovido pelo Laboratório Nacional de Metrologia das Radiações Ionizantes do Instituto de Radioproteção e Dosimetria. MATERIAIS E MÉTODOS: O desempenho foi avaliado em relação ao critério de aceitação de ± 10% de exatidão exigido pela norma brasileira e também aos critérios estabelecidos pela ISO/IEC Guide 43-1, e classificado como "aceitável" ou "não aceitável". Amostras de $^{99}Tc^{m}$ usadas nas comparações foram fornecidas por alguns dos participantes e calibradas no Laboratório Nacional de Metrologia das Radiações Ionizantes para determinar o valor de referência da atividade. RESULTADOS: Esta comparação com o $^{99}Tc^{m}$ mostrou que o desempenho aceitável atendendo à exigência da norma regulatória foi de 82,5%, enquanto pelos critérios estabelecidos pela norma ISO/IEC 43-1 foi de 81,0%. Por outro lado, calibradores de radionuclídeos com detector Geiger-Müller apresentaram desempenho inferior quando comparados com os dotados com câmara de ionização. CONCLUSÃO: Nesta comparação, a avaliação do desempenho baseada nos critérios da ISO/IEC 43-1, os quais são aplicados a laboratórios analíticos, apesar de serem mais restritivas, foi bastante consistente com o critério de exatidão exigido pela norma nacional.**

Unitermos: Teste de proficiência; Calibrador de radionuclídeo; Medicina nuclear; $^{99}Tc^{m}$.

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INTRODUCTION

The field of radionuclide metrology plays an important role in the life sciences activities. Due to the recognition of the quality assurance programs implementation to assure accuracy, repeatability and measurements consistency, it is easy to understand its applicability in nuclear medicine practices[1-4]. The availability of standards with metrological traceability to calibrate instruments and evaluating the performance of activity measurements allows the establishment of quality assurance programs in the use of radiopharmaceuticals. In nuclear medicine centers (NMCs) many types of radioactive substances are utilized in the diagnosis and therapy routines. The instrument utilized for measuring these radiopharmaceuticals activity is the radionuclide calibrator also known as curimeter or dose calibrator. This instru-

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ment comprises an ionization chamber or Geiger-Müller detector coupled with an electrometer with a display whose reading is the activity measured in MBq or Ci submultiples.

The International Atomic Energy Agency[5] and the European Pharmacopoeia[6] recommend a maximum deviation of ± 5% when referring to accuracy of activity measurements with radionuclide calibrators. In Brazil, the accuracy for diagnostic studies is established by the NN.3.05 Standard of the Comissão Nacional de Energia Nuclear (CNEN)[7], which establishes a maximum deviation of ± 10%. The activity delivered to patients must be the closest possible to that prescribed by the physician. If this activity is underestimated, the patient will probably need an additional dose in order to achieve the desired clinical outcome (a good image for diagnosis, for example), resulting in an undesirable dose. If overestimated, the patient will receive an unnecessary dose, and in both cases one of the fundamental principles of radioprotection, that of optimization will be broken.

With the purpose of analyzing the performance of routine activity measurements at the Brazilian NMCs, the Laboratório Nacional de Metrologia das Radiações Ionizantes do Instituto de Radioproteção e Dosimetria/Comissão Nacional de Energia Nuclear (LNMRI-IRD/CNEN) coordinates and organizes programs for comparison of activity measurements of pharmaceutical products utilized in nuclear medicine practices[8]. The participation in such programs occurs on a voluntary basis and is open to all nuclear medicine centers of clinics and hospitals in Brazil. According to the General Coordination of Medicine and Industry of CNEN, there are approximately 300 NMCs in Brazil, 60% of which are in the Southeast region. In the comparison for $^{99}Tc^{m}$ this year, 55 NMCs participated, 34 in the state of Rio de Janeiro, 11 in the city of Porto Alegre, and 10 in Brasília.

In the present study, the criteria of the ISO/IEC 43-1[9] standard were applied, with the objective of homogenizing the procedures for evaluating the performance of the participants in the comparison. The performance evaluation was also carried out by using the *R* rate value of the participating NMC and the result obtained by the LNMRI was adopted as a reference value. Then, the *R* rate is compared with the normative requirements established by the Brazilian regulatory authority[7].

The two evaluation procedures focus mainly on the accuracy and repeatability of measurements and both include the total combined uncertainty associated with measurements from participants, as well the reference value determined by LNMRI. Besides that, two other statistical parameters, the Z_{score}, and the relative deviation were calculated to complement the required information for the performance analysis. According to ISO/IEC 43-1 criteria, for a participant's performance to be considered as "acceptable" all the individual criteria (with the exception of R) must be "acceptable".

MATERIALS AND METHODS

The proficiency test for performance evaluation was applied to the results of activity measured by the 55 NMCs participating in the comparison. The reference value and associated uncertainty were determined by LNMRI utilizing a Centronic IG12 secondary standard ionization chamber calibrated with a standard $^{99}Tc^{m}$ source, which is the standard in primary measurement systems installed at LNMRI.

The final result of the performance evaluation was defined by the combined results of *accuracy*, *repeatability*, *relative deviation* and Z_{score}[9]. Using this approach, the evaluation was applied to the 63 results provided by the participants in the comparison. A code was attributed to each participant, in order to protect their confidentiality.

The value of the *R* rate ($value_{NMC}$/$value_{LNMRI}$) was also determined with the objective of comparing the performance with the acceptance criterion established by the Brazilian standard. In this case the acceptance criterion (or compliance) is $0.90 \leq R \leq 1.10$.

The evaluation and compliance criteria established by ISO/IEC 43-1 are shown in Table 1, where: $value_{LNMRI}$ = reference value determined by LNMRI; $value_{NMC}$ = value determined by the NMC; u_{LNMRI} = standard uncertainty of the reference value; u_{NMC} = standard uncertainty of the NMC value; k = statistical coverage factor (in this study k = 3 was used, for a confidence level of 99.7%; the CNEN NN-3.05 standard requires a 90% confidence level).

RESULTS

Table 2 presents the types and numbers of radionuclide calibrators participating in the comparison, in which one notices a prevalence of the model manufactured by Capintec, followed by the model from Victoreen. The results distribution by region and radionuclide calibrator type (ionization chamber or Geiger-Müller detector) utilized by the participants is presented on Table 3. In percentages, Rio de Janeiro has a larger presence of calibrators with Gei-

Table 1 Statistical criteria adopted for performance evaluation according with ISO/IEC 43-1 standard.

Criterion	Calculated value	Compliance criterion
Accuracy (U_{score})	$U_{score} = \left\| \frac{value_{LNMRI} - value_{SMN}}{k.\sqrt{u^2_{LNMRI} + u^2_{SMN}}} \right\|$	$\|U_{score}\| < 1$
Repeatability (P)	$P = \sqrt{(\frac{u_{LNMRI}}{value_{LNMRI}})^2 + (\frac{u_{SMN}}{value_{SMN}})^2} \times 100\%$	$P \leq \pm 5\%$
Relative deviation (RD)	$RD = \frac{value_{SMN} - value_{LMNRI}}{value_{LNMRI}} \times 100\%$	$RD \leq \pm 10\%$
Z_{score}	$Z_{score} = \frac{value_{SMN} - value_{LMNRI}}{\sigma}$ $\sigma = 0.05 \times value_{LNMRI}$	$2 \leq \|Z_{score}\| \leq 2$

Table 2 Types of radionuclide calibrators utilized by the nuclear medicine centers in the comparison.

Model	Quantity	Participation (%)
CGR Actividigit	2	3.2%
Alfanuclear	4	6.3%
Vexcal	7	11.1%
Atomlab	9	14.3%
Victoreen	14	22.2%
Capintec	27	42.9%
Total	63	100%

Table 4 Nuclear medicine centers performance according with criteria of standards ISO/IEC 43-1 and CNEN NN-3.05.

Evaluation criterion	Acceptable performance (%)
Accuracy (k = 3)	79.4
Repeatability	100
Relative deviation	82.5
Z_{score}	92.1
Performance according with ISO/IEC 43-1	81.0
Performance according with NN-3.05	82.5

ger-Müller detectors (16 in 41, or 39%), while both Brasilia and Porto Alegre have only two in 11 (18%). These figures may explain the inferior performance from participants in Rio de Janeiro (33 acceptable results in 41, or 80%) compared with 10 in 11, or 91% in Brasília, and 100% in Porto Alegre.

Table 4 presents the results of performance evaluations based on ISO/IEC 43-1 criteria and the *R* rate according to the CNEN standard criterion. The performance according to ISO/IEC 43-1 criteria achieved 81% while 82.5% were considered "acceptable" or "compliant", according to the Brazilian standard.

The participants' performances in terms of *R* rate, complying with the accuracy criterion established by the CNEN NN-3.05 standard, are shown on Figure 1. According to this criterion, deviations greater than ± 10%, that is, $0.90 \leq R \leq 1.10$, indicate that the value of the activity determined by a NMC was "non-acceptable" or "noncompliant" according with this standard requirement. The frequency of *R* rate values distribution is shown on Figure 2.

Table 3 Distribution of the results by region and type of radionuclide calibrator (ionization chamber or Geiger-Müller).

Region	Quantity	Calibrator type	
		Ionization chamber	Geiger-Müller detector
Rio de Janeiro	41	25	16
Brasília	11	10	1
Porto Alegre	11	9	2
Total	63	44	19

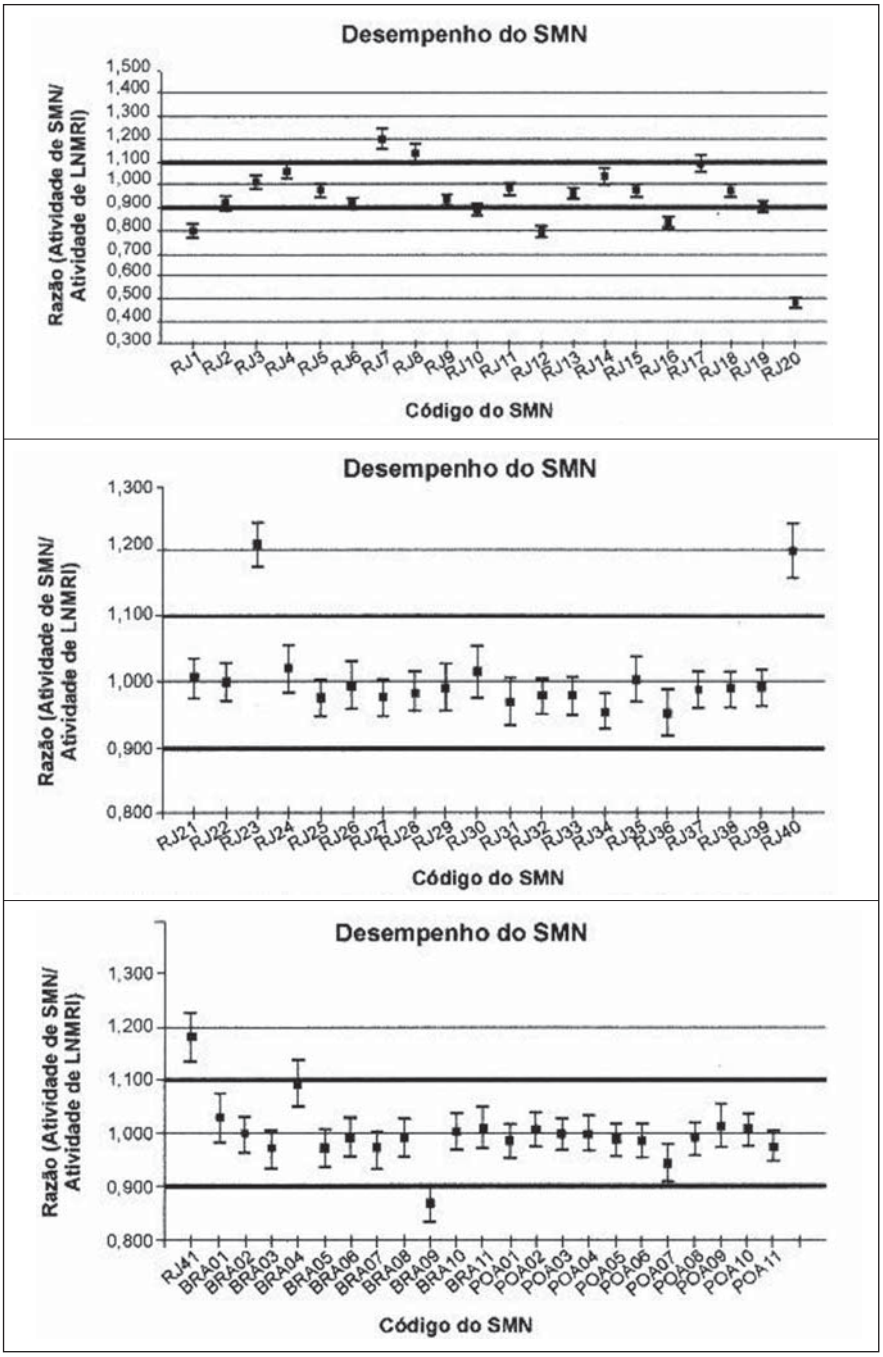

Figure 1. Performance of the 55 participants in terms of *R* rate according with the CNEN NN-3.05 standard. The performance is considered as acceptable (or compliant) when *R* is between 0.90 and 1.10.

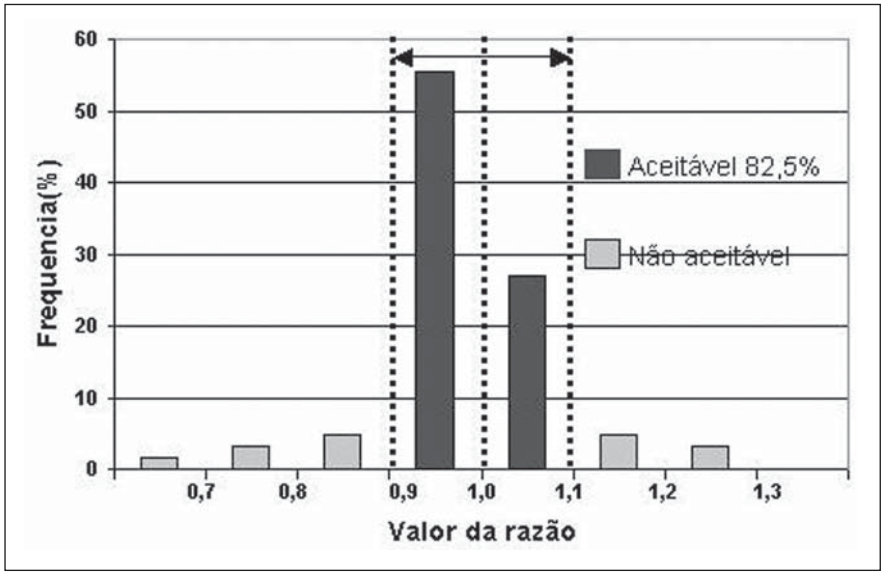

Figure 2. Distribution frequency of the *R* rate values.

DISCUSSION

As some NMCs have more than one radionuclide calibrator, the number of results (63) is larger than the number of participants (55). On Table 3, the fact that Rio de Janeiro, on a percentage basis, has a higher number of calibrators with Geiger-Müller detectors than Brasília and Porto Alegre is evidenced. On Figure 1, one observes that the participant RJ20 presents the largest deviation, with $R = 0.483$, that is, the reading of the activity is underestimated by almost 50%. This fact was known by the participant before the comparison, and the LNMRI was informed that all activity readings for $^{99}Tc^{m}$ were multiplied by 2 in the working routine of this service.

The accuracy evaluated by the U_{score} values, calculated with k = 3 for this comparison, indicates that 81% of the results are "acceptable" and it is consistent with the 82.5% of the values considered as "acceptable" for *relative deviation*. Normally a more strict coverage factor k = 1.96 is utilized for the evaluation of analytical laboratories. As the NMCs are not in this category, k = 3 was utilized in this comparison. If k = 1.96 were utilized, the evaluation under this criterion would be reduced to 71.4%. The *relative deviation* values are equivalent to the *R* rate values that classify the performance according with the criterion set by the Brazilian standard. The evaluation for the *repeatability* criterion demonstrated that 100% of the results presented values lower than ± 5%, indicating a good repeatability of the measurements performed by the NMCs. In what concerns the Z_{score} criterion 92.1% of the results were considered as "acceptable". The mean value for *R*, excluding the RJ20 participant, was evaluated at 0.993 ± 0.079 (8.0%), indicating a slight tendency towards underestimation of activity readings by the participants.

Radionuclide calibrators equipped with Geiger-Müller detectors represent 30% of the instruments in the comparison. By using the *R* rate value to evaluate the performance of the calibrators equipped with Geiger-Müller detector, 70% of the results are classified as "acceptable". On the other hand, the performance of the calibrators equipped with ionization chambers, comprising 70% of the instruments, achieved a value of 88%. This demonstrates that the calibrators with ionization chambers presented a superior performance when compared with the calibrators with Geiger-Müller detector in this comparison. This tendency is also observed in the comparison of the performance by region: 80% of acceptable results for Rio de Janeiro, where the proportion of calibrators with Geiger-Müller detectors is higher, 91% for Brasília and 100% for Porto Alegre. This low performance level can be explained by the configuration of the Geiger-Müller detector in the construction of the calibrator, in which the geometrical dependency is very high.

Finally, the combined use of these four statistical criteria for the proficiency test based on the ISO/IEC 43-1 indicates that the 63 results of the measurements of $^{99}Tc^{m}$ activity obtained in the comparison with the participation of 55 NMCs reached a result of 81% with the "acceptable" classification. This result is quite consistent with the 82.5% obtained for the *R* rate values, complying with the accuracy criteria established by the Brazilian regulatory standard.

CONCLUSIONS

The number of participants in this comparison, 55, corresponding to 18% of the total number of NMCs existing in Brazil (300), is not statistically significant to support a more consistent conclusion. This fact implies the need for greater motivation to encourage NMCs to participate in this type of comparisons. However, it may be concluded that the performance of the radionuclide calibrators utilized by the participants, with 82.5% complying with the requirements of the regulatory standard, was satisfactory. Additionally, a lower performance was expected when the statistical criteria of the ISO/IEC 43-1 were adopted, remembering that such criteria are applicable to analytical laboratories. However, if the coverage factor k = 3 were utilized instead of k = 1.96 in the calculation of the U_{score} values, the performance changes from 71.4% to 81.0%, which is very close to the requirement of the regulatory standard.. This demonstrates that at least in this comparison with $^{99}Tc^{m}$, the quality of the participants' measurements is reasonably satisfactory.

Another conclusion is related to the radionuclide calibrators with Geiger-Müller detectors, which presented lesser "acceptable" performances than those equipped with ionization chambers: 70% and 88% respectively. Such results may support the regulatory authorities in recommending a progressive replacement of the calibrators using Geiger-Müller detectors by calibrators with ionization chambers in order to

improve the overall quality of measurements of radiopharmaceuticals activity at the NMCs. This comparison exercise also establishes traceability in the measurements of radiopharmaceuticals activity and can be utilized to implement corrective and preventive measures in order to improve the quality of services provided to patients.

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