Original article

Dose Calibrator Linearity Testing: Radioisotope ^{99m}Tc or ^{18}F? An Alternative for Reducing Costs in Nuclear Medicine Quality Control

José Willegaignon[1,2], Marcelo T. Sapienza[1,2], George Barberio Coura-Filho[1,2], Alexandre T. Garcez[1,2], Carlos E. Alves[3], Marissa R. Cardona[3], Ricardo F. Gutterres[3], Carlos A. Buchpiguel[1,2]

[1]Nuclear Medicine Service, Cancer Institute of São Paulo State, [2]Nuclear Medicine Service, Institute of Radiology, Clinical Hospital, School of Medicine, University of São Paulo, São Paulo, SP, [3]National Commission on Nuclear Energy (CNEN), Rio de Janeiro, RJ, Brazil

Abstract

Dose calibrator linearity testing is indispensable for evaluating the capacity of this equipment in measuring radioisotope activities at different magnitudes, a fundamental aspect of the daily routine of a nuclear medicine department, and with an impact on patient exposure. The main aims of this study were to evaluate the feasibility of substituting the radioisotope Fluorine-18 (^{18}F) with Technetium-99m (^{99m}Tc) in this test, and to indicate it with the lowest operational cost. The test was applied with sources of ^{99m}Tc (62 GBq) and ^{18}F (12 GBq), the activities of which were measured at different times, with the equipment preadjusted to measuring sources of ^{99m}Tc, ^{18}F, Gallium-67 (^{67}Ga), and Iodine-131 (^{131}I). Over time, the average deviation between measured and expected activities from ^{99m}Tc and ^{18}F were, respectively, 0.56 (±1.79)% and 0.92 (±1.19)%. The average ratios for 99^{m}Tc source experimental activity, when measured with the equipment adjusted for measuring ^{18}F, ^{67}Ga, and ^{131}I sources, in real values, were, respectively, 3.42 (±0.06), 1.45 (±0.03), and 1.13 (±0.02), and those for the ^{18}F source experimental activity, measured through adjustments of ^{99m}Tc, ^{67}Ga, and ^{131}I, were, respectively, 0.295 (±0.004), 0.335 (±0.007), and 0.426 (±0.006). The adjustment of a simple exponential function for describing ^{99m}Tc and ^{18}F experimental activities facilitated the calculation of the physical half-lives of the radioisotopes, with a difference of about 1% in relation to the values described in the literature. Linearity test results, when using ^{99m}Tc, through being compatible with those acquired with ^{18}F, imply the possibility of using both radioisotopes during linearity testing. Nevertheless, this information, along with the high potential of exposure and the high cost of ^{18}F, implies that ^{99m}Tc should preferably be employed for linearity testing in clinics that normally use ^{18}F, without the risk of prejudicing either the procedure itself or the guarantee of a high-quality nuclear medicine service.

Keywords: Dose calibrator, linearity test, nuclear instrumentation, nuclear medicine

Introduction

Dose calibrators are indispensable in the area of nuclear medicine, where they are widely used to measure the amount of radioisotopes to be administered to patients during diagnostic or therapeutic procedures. Routine performance tests are indispensable for evaluating and maintaining equipment efficiency. Among these tests, linearity testing comes to the fore[1] when evaluating the long-term prevalence of the capacity for measuring radioisotope activities at different magnitudes, due to the possibility of variation in the amounts used in diagnostic and therapeutic procedures.

The importance of linearity testing and the technical procedures for its execution[1-4] have been widely discussed in the literature. The aim here is to evaluate equipment linear-response, as produced by the

Access this article online

Quick Response Code:

Website:
www.wjnm.org

DOI:
10.4103/1450-1147.163245

Address for correspondence:
Dr. José Willegaignon, Nuclear Medicine Service, Instituto de Radiologia, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil. E-mail: willegaignon@hotmail.com

different activities of a given radioisotope, from a source with activity close to the minimum resolution of the measuring system (MBq) till that of high activity (GBq). In practice, one can generally start from a high-activity source that will decrease in accordance with the physical decay of the radioisotope employed. Even though linearity testing can be done by using various different isotopes, technetium-99m (^{99m}Tc) has been chosen due to its short physical half-life (6 h), easy obtainment, low cost, and through being the most diffused among nuclear medicine clinics. Moreover, the rising number of clinics dedicated to undertaking tomography with positron emitters, using mainly ^{18}F, which has a higher cost, has led to the possibility of resorting to ^{99m}Tc for linearity testing being contemplated. Thus, the main aims herein are to evaluate the feasibility of substituting the radioisotope ^{18}F with ^{99m}Tc in dose calibrator linearity testing, and to indicate it with the lowest operational cost for nuclear medicine clinics.

Materials and Methods

Linearity testing was undertaken with the activities of ^{99m}Tc and ^{18}F, by means of a CRC-25R dose calibrator, series number 252090 (Capintec Inc., USA), of the Nuclear Medicine Department of Cancer Institute at the School of Medicine, University of São Paulo, Brazil. The equipment is based on a pressurized ionization chamber, presenting appropriate characteristics for use in the area of nuclear medicine. Tests of precision, accuracy, source geometry, and daily controls were first carried out with the calibrator, thereby guaranteeing the high quality of the equipment before starting the present study.

The ^{99m}Tc (62 GBq) source, obtained by elution of the ^{99}Mo/^{99m}Tc- number 350IP0039 generator, São Paulo, SP was acquired from the Nuclear and Energy Research Institute (IPEN). The ^{18}F (12 GBq) batch 131213-0101 source was produced by the cyclotron of the Institute of Radiology of Clinical Hospital, School of Medicine, University of São Paulo, Brazil and donated by the same. Both of the radioisotopes, with the respective volumes of 6.0 mL and 2.5 mL, were in physical liquid form and enclosed in glass flasks.

The ^{99m}Tc source was measured over 5 days and the ^{18}F was measured over 2 days, starting from an initial activity of 62 GBq and 12 GBq, respectively, which generated 13 points of measurement for the ^{99m}Tc source and 10 points of measurement for the ^{18}F. The activity considered at each point was the arithmetic average of 5 measurements. ^{99m}Tc and ^{18}F activities were measured until they reached values compatible with the lowest resolution of the measuring system, as indicated by the manufacturer (~1 MBq), and the values were in accordance with the minimum activity to be used in the test, as indicated.[4-7]

The methodology adopted for evaluating the linearity of detector response in relation to the variation in source activities was the decay method, which consists of measuring the activity of a given source over time, thereby enabling construction of the graph "activity versus time," and comparing the values of experimental activities with the values expected for the same source at different times of measurement. The physical half-lives of ^{99m}Tc (6 h) and ^{18}F (1.83 h) were taken into consideration when calculating expected activities.[6] The acceptable limits for deviation between expected and experimental values were ± 5% and ± 10%, respectively, which are in accordance with the recommendations of the International Atomic Energy Agency (IAEA) and the norms of the Brazilian National Commission on Nuclear Energy (CNEN).[3,4,8]

Both the ^{99m}Tc source and the ^{18}F source were measured with equipment preadjusted for measuring sources of ^{99m}Tc, ^{18}F, Gallium-67 (^{67}Ga), and Iodine-131 (^{131}I), thereby facilitating the comparison of the detector response for one and the same radioactive source, when measured at various different calibrations.

The costs of purchasing the required ^{99m}Tc and ^{18}F sources specifically for linearity testing were also investigated in the Brazilian market.

In this sense, and when necessary, some data are presented in the form of average value ± 1 standard deviation (SD).

Results

Successive measurements of ^{99m}Tc and ^{18}F sources experimentally showed that, according to the time, temporal variation in their activities was consequentially linked to the radioactive disintegration process. All experimental measurements and their respective ratios are presented in Tables 1 and 2, and the different trends for obtained values, in Figures 1 and 3. Swerves correspond to deviation between the value of the experimental activities acquired with the dose calibrator, and that theoretically and simultaneously expected for the source, at the time of measurement.

It is important to note that the experimental activities indicated in the tables and figures represent the average of a series of five measurements. As a result of the high level of equipment accuracy, the SD presented in each measurement series was around 1% of the average value for the set of measurements as a whole.

Figures 2 and 4 show deviation dispersion between the experimental and theoretical values of ^{99m}Tc and ^{18}F sources, according to time, as well as the

Table 1: Ratios and deviation between the experimental and expected activities for ^{99m}Tc source, when measured at different times and points in calibrator adjustment

Date and time of measurement (mm/dd/aa-h)	Calibration				Ratio ^{99m}Tc/^{18}F	Ratio ^{99m}Tc/^{67}Ga	Ratio ^{99m}Tc/^{131}I	Deviation* (%)
	^{99m}Tc [MBq]	^{18}F [MBq]	^{67}Ga [MBq]	^{131}I [MBq]				
12/08/2013 09:02	62,345.00	18,337.20	55,204.00	43,401.00	3.40	1.129	1.436	0.00
12/08/2013 20:02	17,301.20	5,088.24	15,369.80	12,017.60	3.40	1.126	1.440	1.13
12/09/2013 08:16	4,184.70	1,232.10	3,715.54	2,903.76	3.40	1.126	1.441	1.76
12/09/2013 18:25	1,295.74	380.80	1,148.48	896.88	3.40	1.128	1.445	1.77
12/10/2013 08:06	267.88	78.37	236.73	184.70	3.42	1.132	1.450	1.36
12/10/2013 11:50	174.42	51.25	148.52	116.70	3.40	1.174	1.495	1.15
12/10/2013 17:47	87.54	25.79	77.55	61.01	3.40	1.129	1.435	1.36
12/11/2013 08:25	16.14	4.74	14.19	11.20	3.40	1.137	1.442	1.43
12/11/2013 15:11	7.46	2.18	6.60	5.19	3.42	1.130	1.438	0.47
12/11/2013 18:50	4.84	1.44	4.30	3.38	3.36	1.126	1.431	1.56
12/12/2013 07:53	1.14	0.33	1.02	0.80	3.50	1.116	1.426	−4.65
12/12/2013 14:37	0.50	0.14	0.43	0.33	3.58	1.172	1.511	−0.57
12/12/2013 18:56	0.28	0.08	0.25	0.20	3.45	1.118	1.407	7.47
General average					3.42±0.06	1.45±0.03	1.13±0.02	1.10±2.57

*Deviation between the experimental and expected activity for ^{99m}Tc source

Table 2: Ratios and deviation between experimental and expected activities for ^{18}F source, when measured at different times and points in calibrator adjustment

Date and time of measurement (mm/dd/aa - h)	Calibration				Ratio ^{18}F/^{99m}Tc	Ratio ^{18}F/^{67}Ga	Ratio ^{18}F/^{131}I	Deviation* (%)
	^{99m}Tc [MBq]	^{18}F [MBq]	^{67}Ga [MBq]	^{131}I [MBq]				
12/13/2013 06:50	40,293.00	11,928.80	35,594.00	28,009.00	0.296	0.335	0.426	0.00
12/13/2013 08:18	23,014.00	6,803.56	20,142.80	15,961.80	0.296	0.338	0.426	0.61
12/13/2013 11:15	7,339.32	2,200.02	6,435.04	5,074.92	0.300	0.342	0.434	1.77
12/13/2013 12:25	4,926.92	1,459.28	4,383.02	3,405.48	0.296	0.333	0.429	-1.35
12/13/2013 14:18	2,385.02	687.61	2,102.34	1,648.72	0.288	0.327	0.417	2.55
12/13/2013 15:20	1,610.98	467.24	1,428.20	1,117.40	0.290	0.327	0.418	2.07
12/13/2013 16:25	1,084.84	315.24	971.62	748.14	0.291	0.324	0.421	0.42
12/13/2013 18:00	579.42	171.24	511.56	402.78	0.296	0.335	0.425	1.47
12/13/2013 23:18	77.48	23.18	68.34	53.50	0.299	0.339	0.433	0.76
12/14/2013 10:48	0.94	0.28	0.81	0.65	0.299	0.349	0.432	6.24
General average					0.295±0.004	0.335±0.007	0.426±0.006	1.45±2.02

*Deviation between the experimental and expected activity for ^{18}F source

Table 3: The physical half-lives of ^{99m}Tc and ^{18}F furnished through the adjustment of an exponential function for the activities indicated by the equipment, when ^{99m}Tc and ^{18}F sources are measured at different times and with dose calibrator adjustment

Calibration	Radioactive Source: ^{99m}Tc				Radioactive Source: ^{18}F			
	λ	R^2	Physical half-life	Deviation*	λ	R^2	Physical half-life	Deviation*
^{99m}Tc	0.11649±0.00005	1	5.949±0.003	0.85%	0.3822±0.0019	1	1.813±0.009	0.93%
^{18}F	0.11649±0.00005	1	5.949±0.003	0.85%	0.3816±0.0015	1	1.816±0.007	0.77%
^{67}Ga	0.11622±0.00002	1	5.9628±0.0010	0.62%	0.3853±0.0029	1	1.799±0.008	1.69%
^{131}I	0.11667±0.00005	1	5.940±0.003	1.00%	0.3836±0.0020	1	1.807±0.009	1.26%

*Deviation between the value calculated with the experimental data and the theoretical data from the literature[6]

acceptable lower and upper limits for linearity testing, in accordance with IAEA and CNEN norms.

The average deviation between experimental and expected activities for the ^{99m}Tc and ^{18}F sources was, respectively, 1.10 (±2.57)% and 1.45 (±2.02)%, and the respective maximum values encountered were 7.47% (^{99m}Tc) and 6.24% (^{18}F), both of which were situated at the lowest limit of minimum resolution of the measuring system (<1 MBq). In the case of activity values higher than the lowest limit, average deviation was 0.56 (±1.79)% for the ^{99m}Tc source and 0.92 (±1.19)% for the ^{18}F source, thereby clearly indicating the excellent quality of the system for measuring the different amount of activities of a single radioisotope.

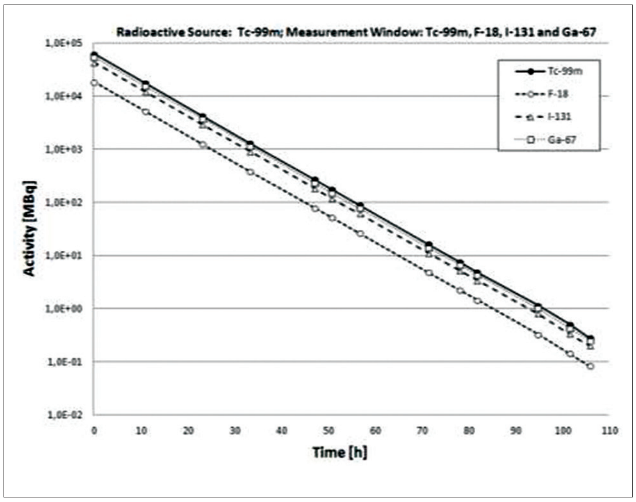

Figure 1: Trend of the values of activities from ^{18}F source, when measured with equipment preadjusted for measuring ^{18}F, ^{99m}Tc, ^{131}I, and ^{67}Ga sources

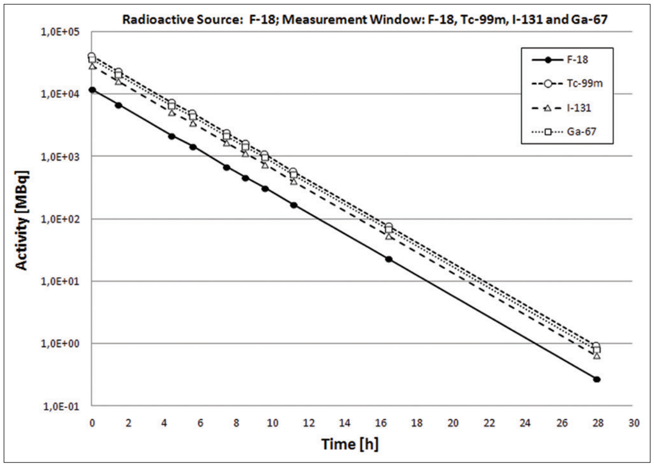

Figure 3: Trend of the values of activities from ^{18}F source, when measured with equipment preadjusted for measuring ^{18}F, ^{99m}Tc, ^{131}I, and ^{67}Ga sources

Adjustment of exponential functions of the type , $y = a + b^{-\lambda t}$ where, $\lambda = 0.693 / T_{1/2\,phys}$,for experimental data from the ^{99m}Tc and ^{18}F sources facilitated calculation of the physical half-lives of both radioisotopes, which in this case were, respectively, 5.949 (±0.002) and 1.816 (±0.007) h, with a difference of about 1% in relation to the values indicated in the literature.[6] Table 3 shows the physical half-lives of the radioisotopes (^{99m}Tc and ^{18}F) calculated by using experimental activities acquired when these sources were measured with the equipment preadjusted for measuring ^{99m}Tc, ^{18}F, ^{67}Ga, and ^{131}I sources.

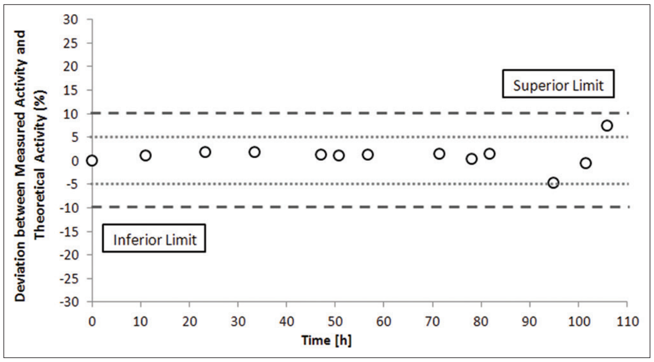

Figure 2: Deviation dispersion between the experimental and theoretical values of activities from ^{99m}Tc source, as related to time, including the lowest and uppermost limits acceptable for the test

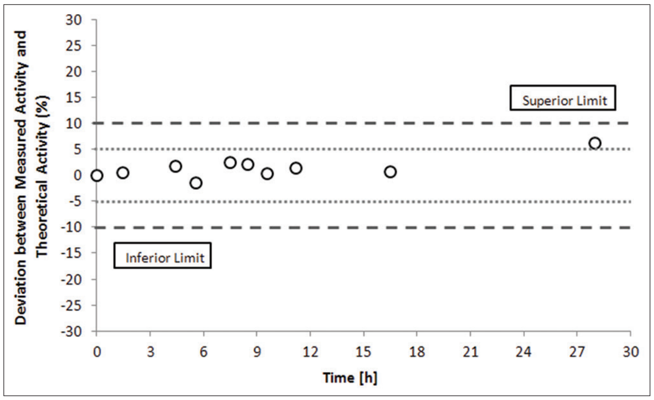

Figure 4: Deviation dispersion between the experimental and theoretical values of activities from ^{18}F source, according to time, and including the lowest and uppermost limits acceptable for the test

The average ratios for the real activity of the ^{99m}Tc source and those indicated by the equipment, when this source was measured with equipment preadjusted for measuring ^{18}F, ^{67}Ga, and ^{131}I sources were, respectively, 3.42 (±0.06), 1.45 (±0.03), and 1.13 (±0.02), and those for the ^{18}F source when measuring ^{99m}Tc, ^{67}Ga, and ^{131}I sources were, respectively, 0.295 (±0.004), 0.335 (±0.007), and 0.426 (±0.006). Figures 5 and 6 represent the trends for the ratios encountered. These trends were considered to be constant throughout all the measurement points [Tables 1 and 2], thereby implying the possibility of using both radioisotopes when carrying out linearity testing, independent of the type of calibration used for measuring the source, since the specific aim of this test is to evaluate particular equipment response when measuring the different amounts of activity of one and the same radioisotope, the response of which should be linear during the interval between the lower and upper limits of activities of daily use in a clinic of nuclear medicine.[4]

On considering operational costs, in Brazil the price of a ^{99}Mo/^{99m}Tc generator of 6.75 GBq (250 mCi) for undertaking linearity tests is around US $578.00 and the price for an ^{18}FDG source of 6.75 GBq (250 mCi) is around US $1,556.00. This is according to consultations carried out in May, 2014, and directed to the Nuclear and Energy Research Institute (IPEN), an organ of the

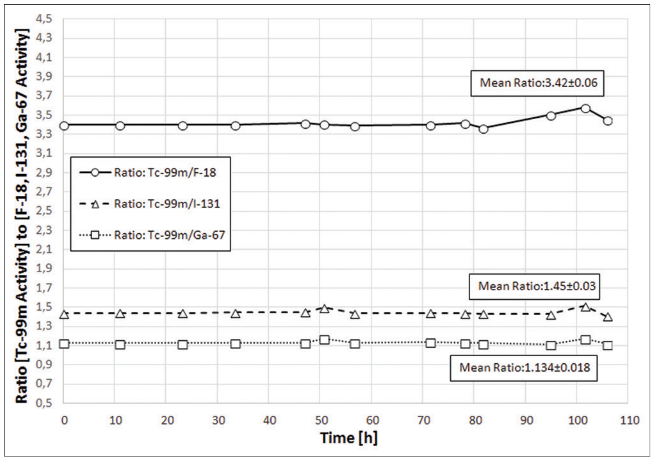

Figure 5: Trend of the values of the ratios between real activities from a ^{99m}Tc source, and those indicated by the equipment, when measuring with equipment preadjusted for measuring ^{18}F, ^{67}Ga, and ^{131}I sources at multiple intervals in time

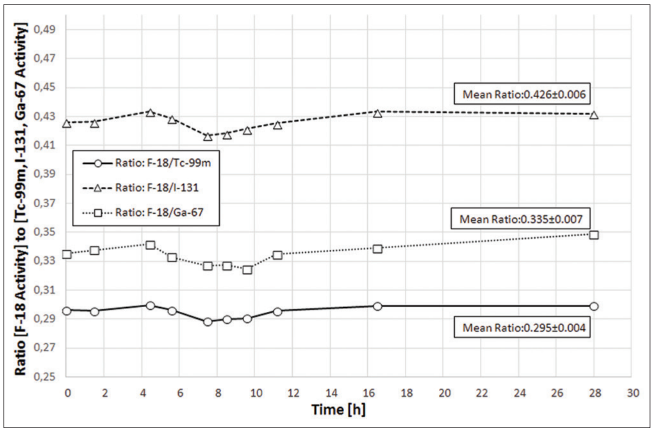

Figure 6: Trend of the values of the ratios between the real activity from ^{18}F source, and those indicated by the equipment, when measuring with equipment preadjusted for measuring ^{99m}Tc, ^{67}Ga, and ^{131}I sources at multiple intervals in time

CNEN, and the main supplier of radioisotopes in the Brazilian market.

Discussion

The electric current generated in a dose calibrator inside an ionization chamber, which is proportional to the activity, is related as much to the amount of radioactive atoms existent in a given sample as to the energy of the photons liberated during the disintegration process. Various radioisotopes obtain the same electric current per unit of activity (pA/MBq, picoampere per MBq), which makes individual radioisotope identification during measurement impossible. Thus, obtainment of a trustworthy reading involves inserting correction factors into the current that are proportional to the radioisotope to be measured. This is achieved automatically by means of the radioisotope selector inside the equipment itself. Generally, factors of correction between one radioisotope and another are constant, having as point of reference the radioisotopes used by the manufacturer during calibration of the equipment, namely, ^{60}Co and ^{137}Cs.[2]

Once the essential characteristics of the measuring system, such as high precision and accuracy, have been maintained and the daily constancy tests kept up, linearity tests generally present good results within the acceptable test limits. In the present study, the tests were carried out using ^{99m}Tc and ^{18}F sources. Both independently showed the excellent quality of the equipment when measuring different amounts of radioisotope activities with very distinct energies, as in the case of 141 keV (^{99m}Tc) and 0.511 MeV (^{18}F)[6] [Figures 2 and 4].

The practically constant ratios between the activities indicated by the equipment for the same source, when measured at different points in calibration [Tables 1 and 2, and Figures 5 and 6], show that the use of a single radioisotope, for example ^{99m}Tc, could be sufficient for resorting to linearity testing, independent of the exclusive use (or not) of ^{18}F by a nuclear medicine clinic. As can be seen in Table 3, this information is reinforced through the similarity in values for the physical half-lives of either ^{99m}Tc or ^{18}F, when these sources were measured in the calibrations of ^{99m}Tc, ^{18}F, ^{67}Ga, and ^{131}I. As was experimentally shown in this study [Tables 1 and 2], conceptually the dose calibrator response can be considered linear if either the ratio or deviation in response, as measured by the estimated response, remains constant over time.[5]

Complementary to the above points, linearity testing functions as a means of evaluating the characteristics of ionization chamber saturation, as well as electrometer linearity, when measuring an electric current. Thus, the test is not directly linked to the radioisotope used but to the amount of electric charges generated during the measuring process. Therefore, this test could be used with various different radioisotopes, once the current interval proportional to the activity interval to be tested is within the limits, as practiced by nuclear medicine clinics. This information is extremely important and useful for clinics that operate exclusively with positron emitters, as in the case of ^{18}F.

As is evident from the AAPM 181 report,[5] the elements chosen for linearity testing have been restricted to ^{99m}Tc and ^{18}F since clinical application of the test with all the available radioisotopes becomes unpractical. Apparently, there is a lack of consensus as to the activities to be employed, a situation in which some recommend testing with activities within the interval where the dose calibrator will be used, while others, such as the IAEA, recommend starting the test with the maximum activity administered to patients within the clinic routine. However, all agree that the minimum activity to be measured should be close to the resolution value of the measuring system (~1 MBq).[5] Moreover, one must consider that not all the measured activities will be administered to the patient, as is the case of the activities that will be stored as liquid radioactive waste, such as the leftovers of noninjected radiopharmaceuticals. In this case, the correct measurement of an activity is of vital importance when considering storage time.

Differences in the purchasing price of the resources required for linearity testing when using either ^{99m}Tc or ^{18}F are very significant, often reaching 40%, taking into consideration the price of radioactive sources alone.

A feasible alternative for a greater reduction in costs would be the acquisition of ^{99m}Tc activities exclusively for linearity testing, directly from the suppliers. This would be a more plausible solution, seeing that the acquisition of a ^{99}Mo/^{99m}Tc generator just for the purpose of linearity testing would be a waste of resources, at an unfavorable moment worldwide, with the present crisis in the radioisotope market. Most certainly, the cost of acquiring a ^{99m}Tc source solely for linearity testing would be lower than that of obtaining a generator, or even free, in the case of logistics and radioisotope supplier predisposition. This would have an enormous impact on the test procedure.

It is noteworthy that the use of ^{99m}Tc sources, instead of ^{18}F sources, would result in a reduction in potential occupational and environmental exposure hazards, since an ^{18}F source presents a dose potential around 10 times greater than that presented by a ^{99m}Tc source of the same activity, namely, 135.1 μGy/GBq.m^2.h and 14.1 μGy/GBq.m^2.h, respectively.[9]

Thus, it was possible to demonstrate the possibility of optimizing linearity testing with a dose calibrator, thereby calling the attention of researchers and regulator agents to a conscientious evaluation of the information presented, seeing that its dissemination can lead to a reduction in costs in the public and private health sectors, without losing focus on continuous evolution in the quality of the health services offered to society as a whole.

Conclusion

The physical characteristics of the dose calibrator used in the present study clearly indicated that the results of linearity testing using ^{99m}Tc are compatible with those acquired using ^{18}F, thereby implying the possibility of employing both indiscriminately when undertaking linearity testing with this type of equipment as well as with others of a like configuration and in satisfactory conditions of use. This information, allied to the high potential of radiation exposure and prices of acquiring ^{18}F, imply that ^{99m}Tc can be employed as a suitable substitute, when applying linearity tests in clinics that normally use ^{18}F, without prejudicing either the procedure or the guarantee of quality of a nuclear medicine service.

References

1. Zanzonico P. Routine quality control of clinical nuclear medicine instrumentation: A brief review. J Nucl Med 2008;49:1114-31.
2. Prekeges J. Nuclear Medicine Instrumentation. 1st ed. USA: Jones and Bartlett Publishers; 2011.
3. International Atomic Energy Agency. Quality control of nuclear medicine instruments. Austria: IAEA-TECDOC-602; 1991.
4. International Atomic Energy Agency. Quality assurance for radioactivity measurement in nuclear medicine. Austria: IAEA-TRS-454; 2006.
5. American Association of Physicists in Medicine. The selection, use, calibration, and quality assurance of radionuclide calibrators used in nuclear medicine. Maryland, United States: AAPM Report No. 181; 2012.
6. National Physical Laboratory. Protocol for establishing and maintaining the calibration of medical radionuclide calibrators and their quality control. Middlesex, United Kingdom: NPL Measurement Good Practice Guide No. 93; 2006.
7. Busemann Sokole E, Płachcínska A, Britten A, Lyra Georgosopoulou M, Tindale W, Klett R. Routine quality control recommendations for nuclear medicine instrumentation. Eur J Nucl Med Mol Imaging 2010;37:662-71.
8. Comissão Nacional de Energia Nuclear. Requisitos de segurança e proteção radiológica para serviços de medicina nuclear. Brazil: CNEN-NN-3.05; 2013.
9. Ninkovic MM, Raicevic JJ, Adrovic F. Air kerma rate constants for gamma emitters used most often in practice. Radiat Prot Dosimetry 2005;115:247.

How to cite this article: Willegaignon J, Sapienza MT, Coura-Filho GB, Garcez AT, Alves CE, Cardona MR, *et al.* Dose Calibrator Linearity Testing: Radioisotope 99mTc or ^{18}F? An Alternative for Reducing Costs in Nuclear Medicine Quality Control. World J Nucl Med 2015;14:165-70.

Source of Support: Nil, **Conflict of Interest:** None declared.