

# Dose calibrator linearity test: $^{99m}\text{Tc}$ versus $^{18}\text{F}$ radioisotopes\*

Teste de linearidade em medidor de atividade: utilização do radioisótopo  $^{99m}\text{Tc}$  versus  $^{18}\text{F}$

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**Abstract Objective:** The present study was aimed at evaluating the viability of replacing  $^{18}\text{F}$  with  $^{99m}\text{Tc}$  in dose calibrator linearity testing. **Materials and Methods:** The test was performed with sources of  $^{99m}\text{Tc}$  (62 GBq) and  $^{18}\text{F}$  (12 GBq) whose activities were measured up to values lower than 1 MBq. Ratios and deviations between experimental and theoretical  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  sources activities were calculated and subsequently compared. **Results:** Mean deviations between experimental and theoretical  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  sources activities were 0.56 ( $\pm$  1.79)% and 0.92 ( $\pm$  1.19)%, respectively. The mean ratio between activities indicated by the device for the  $^{99m}\text{Tc}$  source as measured with the equipment pre-calibrated to measure  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  was 3.42 ( $\pm$  0.06), and for the  $^{18}\text{F}$  source this ratio was 3.39 ( $\pm$  0.05), values considered constant over the measurement time. **Conclusion:** The results of the linearity test using  $^{99m}\text{Tc}$  were compatible with those obtained with the  $^{18}\text{F}$  source, indicating the viability of utilizing both radioisotopes in dose calibrator linearity testing. Such information in association with the high potential of radiation exposure and costs involved in  $^{18}\text{F}$  acquisition suggest  $^{99m}\text{Tc}$  as the element of choice to perform dose calibrator linearity tests in centers that use  $^{18}\text{F}$ , without any detriment to the procedure as well as to the quality of the nuclear medicine service.

**Keywords:** Nuclear medicine; Dose calibrator; Linearity test; Nuclear instrumentation.

**Resumo Objetivo:** Avaliar a viabilidade de substituir o radioisótopo  $^{18}\text{F}$  pelo  $^{99m}\text{Tc}$  no teste de linearidade em medidores de atividade. **Materiais e Métodos:** O teste foi realizado empregando-se fontes de  $^{99m}\text{Tc}$  (62 GBq) e  $^{18}\text{F}$  (12 GBq), cujas atividades foram mensuradas até valores abaixo de 1 MBq. As razões e desvios entre as atividades experimentais e teóricas foram calculados e comparados. **Resultados:** Os desvios médios entre as atividades experimentais e teóricas para o  $^{99m}\text{Tc}$  e  $^{18}\text{F}$  foram, respectivamente, 0,56 ( $\pm$  1,79)% e 0,92 ( $\pm$  1,19)%. A razão média entre as atividades indicadas pelo equipamento para a fonte de  $^{99m}\text{Tc}$  quando mensurada no equipamento pré-ajustado para medir o  $^{99m}\text{Tc}$  e  $^{18}\text{F}$  foi 3,42 ( $\pm$  0,06), e para o  $^{18}\text{F}$  este valor foi 3,39 ( $\pm$  0,05), razões consideradas constantes ao longo de todo o período de medida. **Conclusão:** Os resultados do teste utilizando o  $^{99m}\text{Tc}$  são compatíveis com os adquiridos com o  $^{18}\text{F}$ , implicando na possibilidade de utilização de ambos os radioisótopos na realização do teste de linearidade. Esta informação, aliada ao elevado potencial de exposição e custos de aquisição do  $^{18}\text{F}$ , sugere que o  $^{99m}\text{Tc}$  seja empregado na realização do teste de linearidade para clínicas que utilizam  $^{18}\text{F}$ , sem prejuízo para o procedimento e garantia da qualidade de um serviço de medicina nuclear.

**Unitermos:** Medicina nuclear; Medidor de atividade; Teste de linearidade; Instrumentação nuclear.

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## INTRODUCTION

Dose calibrator is an indispensable equipment in the field of nuclear medicine, and is widely utilized in the measurement of radioisotopes quantities to be administered to patients both in diagnostic and therapeutic procedures. For evaluation and proper maintenance, such an equipment must be routinely submitted to performance tests, particularly the linearity test<sup>(1)</sup>. Such a test is aimed at evaluating whether the equipment maintains its capability of measuring the radioisotopes activities in different magnitudes, as the quanti-

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ties utilized in diagnostic and therapeutic procedures may differ by orders of magnitude.

Several studies in the literature indicate the relevance of the linearity test and the technical procedures for its implementation<sup>(1-4)</sup>. Such a test is aimed at evaluating the linear response of the equipment produced by different activities of a given radioisotope, from a source with an activity close to the minimum resolution of the measurement system (MBq) to a high activity source (GBq). In practice, generally one starts with a high activity source, which will decrease according to the radioisotope physical decay. Although the linearity test may be performed by utilizing different radioisotopes, technetium-99m ( $^{99m}\text{Tc}$ ) has been the element of choice due to its short physical half-life (6 hours), wide availability, low cost and for being the element with higher representativeness at nuclear medicine clinics. On the other hand, the increasing number of clinics dedicated to positron emission tomography, relying mainly on fluoride-18 ( $^{18}\text{F}$ ), has led to questions on the possibility of the utilization of  $^{99m}\text{Tc}$  in linearity tests at such clinics, with a view on the high acquisition cost of  $^{18}\text{F}$ .

Based on the above mentioned factors, the main objective of the present study is evaluating the use of  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  radioisotopes in linearity tests, comparing results and indicating the radioisotope of lowest operational cost for nuclear medicine clinics.

## MATERIALS AND METHODS

The linearity test was performed utilizing  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  sources in a CRC-25R dose calibrator, serial number 252090 (Capintec Inc., USA) of the Nuclear Medicine Service of Instituto do Câncer do Estado de São Paulo Octavio Frias de Oliveira (Icesp). Such an equipment is based on a pressurized ionization chamber, with suitable characteristics for utilization in the field of nuclear medicine. Previously to linearity tests, precision, accuracy, source geometry tests and daily controls were performed in the dose calibrator, assuring the good quality of the equipment before starting the study.

The initial activity of the  $^{99m}\text{Tc}$  source (62 GBq) was obtained by means of  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator elution process, number 350IP0039, acquired under purchasing procedure from Instituto de Pesquisas Energéticas e Nucleares (Ipen). The  $^{18}\text{F}$  source (initial activity of 12 GBq), lot 131213-0101, was acquired by donation from Ciclotron of Instituto de Radiologia do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. Both sources were in the liquid physical state, with respective volumes of 6.0 mL and 2.5 mL, in glass vials.

The  $^{99m}\text{Tc}$  source was measured along five days while the  $^{18}\text{F}$  source was measured along two days, starting from the initial activities of 62 GBq and 12 GBq, respectively, obtaining 13 measurement spots for the  $^{99m}\text{Tc}$  source and 10 spots for the  $^{18}\text{F}$  source. The activity considered for each measurement spot corresponded to the arithmetic mean of

five measurements. The  $^{99m}\text{Tc}$  activity as well as that of  $^{18}\text{F}$  were measured until the activities reached values compatible with the lower resolution of the measurement system, indicated by the manufacturer ( $\sim 1$  MBq) and in accordance with the minimum activity to be utilized in the test and indicated by different recommendations<sup>(4-7)</sup>.

The method adopted to evaluate dose calibrator response linearity in relation to the variation of the sources activities was the decay method, which consists of measuring the activity of a given source along time, allowing for the plotting of the “activity versus time” curve and the comparison of the experimental activity values with the expected theoretical values for the source at the different measurement times. The calculation of the theoretical activities took into consideration the physical half-life of both  $^{99m}\text{Tc}$  (6 hours) and  $^{18}\text{F}$  (1.83 hours)<sup>(6)</sup>. The acceptable limits for deviation between the theoretical and experimental values were  $\pm 5\%$  and  $\pm 10\%$  in accordance with recommendations from International Atomic Energy Agency (IAEA) and standards of Comissão Nacional de Energia Nuclear (CNEN)<sup>(3,4,8)</sup>.

Both the  $^{99m}\text{Tc}$  and the  $^{18}\text{F}$  sources were measured with the equipment being pre-adjusted for the measurement of  $^{99m}\text{Tc}$  sources ( $^{99m}\text{Tc}$  “window”) and subsequently for  $^{18}\text{F}$  sources ( $^{18}\text{F}$  “window”), thus allowing for the comparison of detector response for the same radioactive source when measured at different radioisotope windows.

The acquisition costs of the  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  sources necessary for the linearity tests were also estimated.

In the present study, as necessary, some data are presented as mean value  $\pm 1$  standard deviation.

## RESULTS

Successive measurements of the  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  sources have experimentally demonstrated the variation of their activities over time as result of the radioactive decay process. All the experimental measurements and the ratios between such measurements are presented on Table I, and the trend lines for the obtained values can be observed on Figures 1, 3, 5 and 6. The deviation value presented on the table corresponds to the deviation between the experimental activity value acquired by means of the dose calibrator and that estimated for the source by means of calculation for the same time span.

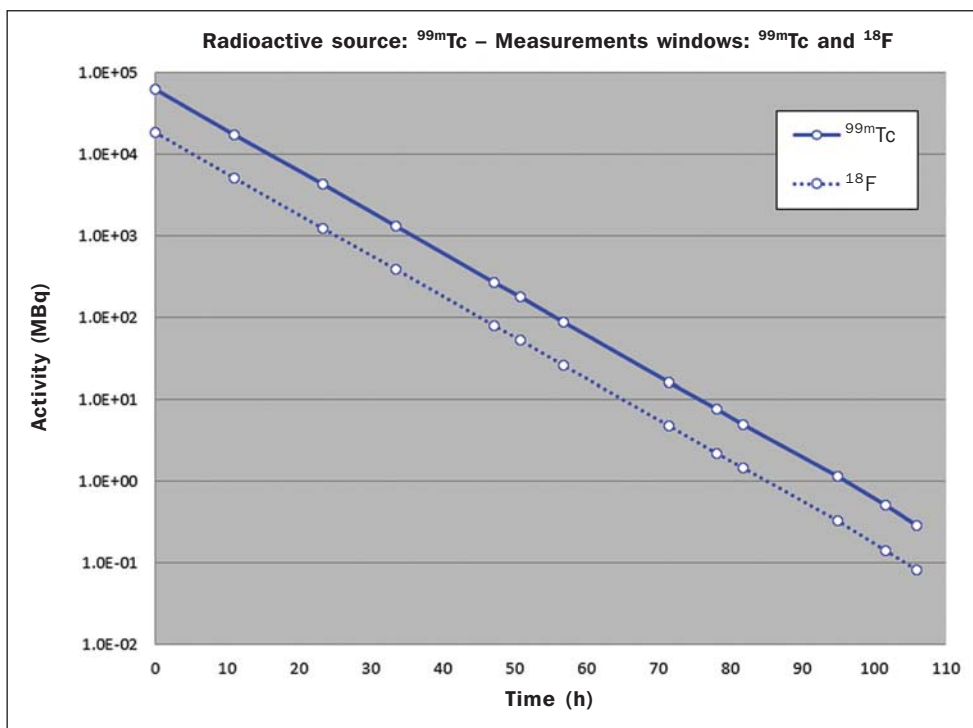
Because of the good precision of the equipment, the standard deviation presented in each measurement series corresponded to approximately 1% of the mean value for that set of measurements.

It is important to emphasize that the experimental activities indicated on the table and figures represent the mean value of a series of five measurements, but the measurements standard deviation (approximately 1% of the mean value) was not indicated in order not to impair or confuse the visual analysis of the charts and table.

Figures 2 and 4 represent the characteristic charts of the linearity test, indicating the relationship between the experi-

**Table** — Ratios and deviations between experimental and theoretical activities for the <sup>99m</sup>Tc and <sup>18</sup>F sources at different times and measurement windows.

Radioactive source: <sup>99m</sup> Tc					Radioactive source: <sup>18</sup> F				
Date – time of measurements	Measurement window		Ratio <sup>99m</sup> Tc/ <sup>18</sup> F	Deviation (%)	Date – time of measurements	Measurement window		Ratio <sup>99m</sup> Tc/ <sup>18</sup> F	Deviation (%)
	<sup>99m</sup> Tc (MBq)	<sup>18</sup> F (MBq)				<sup>18</sup> F (MBq)	<sup>99m</sup> Tc (MBq)		
08/12/2013 – 09:02	62,345.00	18,337.20	3.40	0.00	13/12/2013 – 06:50	11,928.80	40,293.00	3,38	0,00
08/12/2013 – 20:02	17,301.20	5,088.24	3.40	1.13	13/12/2013 – 08:18	6,803.56	23,014.00	3,38	0,61
09/12/2013 – 08:16	4,184.70	1,232.10	3.40	1.76	13/12/2013 – 11:15	2,200.02	7,339.32	3,34	1,77
09/12/2013 – 18:25	1,295.74	380.80	3.40	1.77	13/12/2013 – 12:25	1,459.28	4,926.92	3,38	-1,35
10/12/2013 – 08:06	267.88	78.37	3.42	1.36	13/12/2013 – 14:18	687.61	2,385.02	3,47	2,55
10/12/2013 – 11:50	174.42	51.25	3.40	1.15	13/12/2013 – 15:20	467.24	1,610.98	3,45	2,07
10/12/2013 – 17:47	87.54	25.79	3.40	1.36	13/12/2013 – 16:25	315.24	1,084.84	3,44	0,42
11/12/2013 – 08:25	16.14	4.74	3.40	1.43	13/12/2013 – 18:00	171.24	579.42	3,39	1,47
11/12/2013 – 15:11	7.46	2.18	3.42	0.47	13/12/2013 – 23:18	23.18	77.48	3,34	0,76
11/12/2013 – 18:50	4.84	1.44	3.36	1.56	14/12/2013 – 10:48	0.28	0.94	3,36	6,24
12/12/2013 – 07:53	1.14	0.33	3.50	-4.65					
12/12/2013 – 14:37	0.50	0.14	3.58	-0.57				Overall average	3.39 ± 1.45 ± 0.05 2.02
12/12/2013 – 18:56	0.28	0.08	3.45	7.47					
			Overall average	3.42 ± 1.10 ± 0.06 2.57					



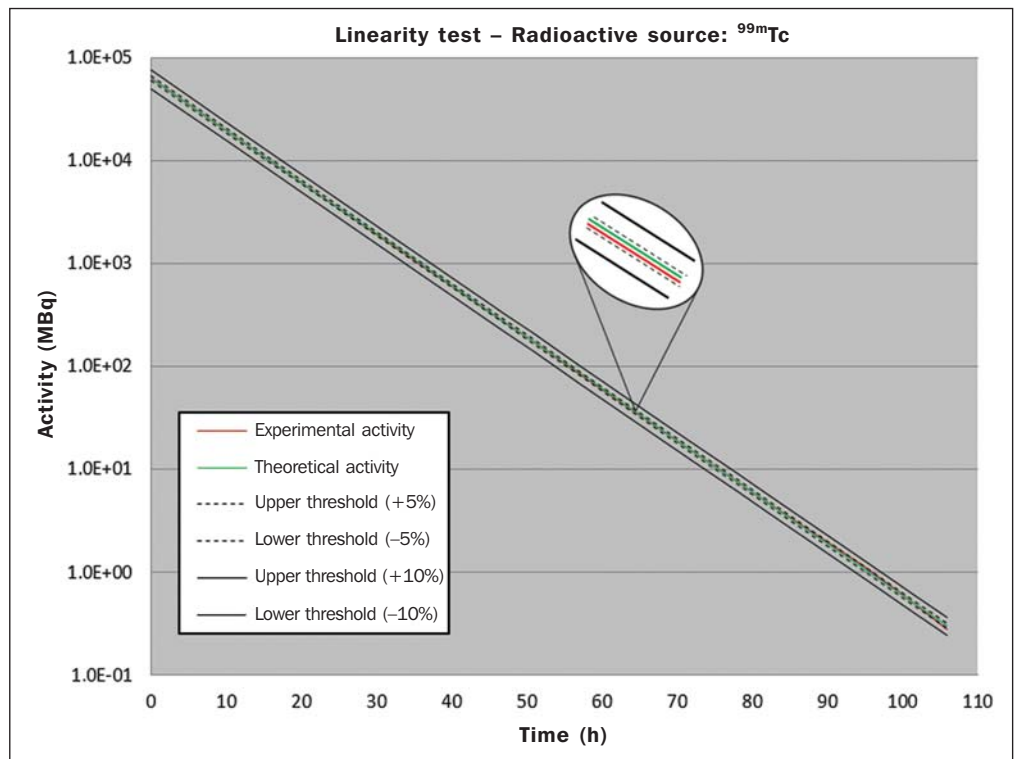
**Figure 1.** <sup>99m</sup>Tc source activity decrease as a function of time as measured in the <sup>99m</sup>Tc and <sup>18</sup>F windows.

mental and theoretical values of the <sup>99m</sup>Tc and <sup>18</sup>F activities as a function of time, as well as the lower and upper acceptable limits for the test in accordance with the IAEA recommendations and CNEN standards.

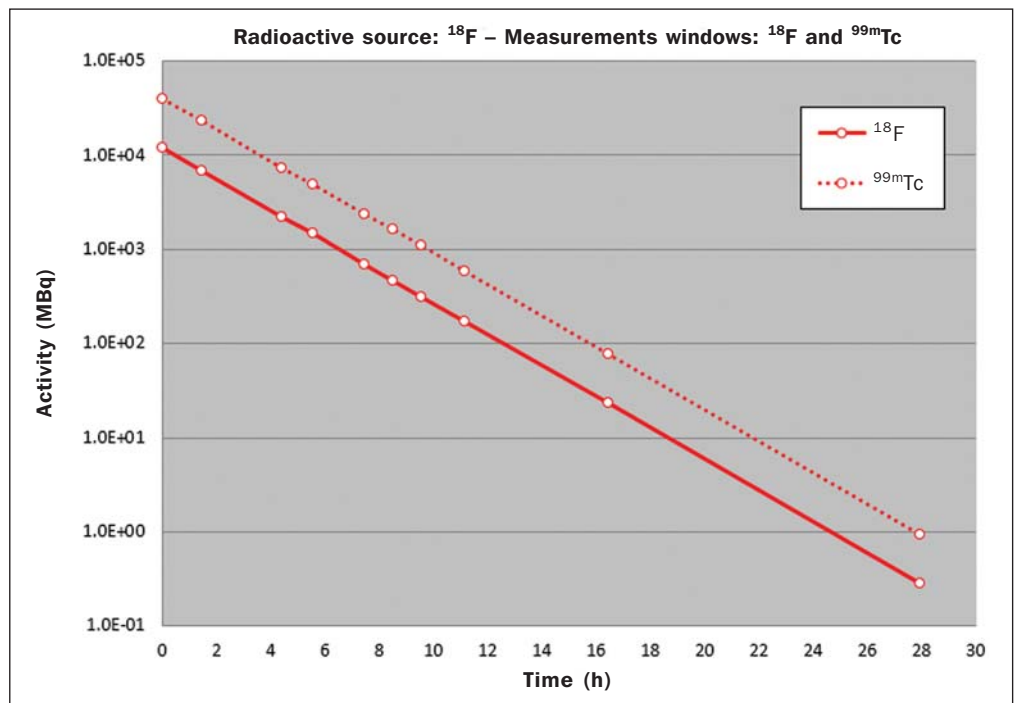
The mean deviation between the experimental and theoretical activities for the <sup>99m</sup>Tc and <sup>18</sup>F sources were, respectively, 1.10 (± 2.57)% and 1.45 (± 2.02)% and the maximum values observed were 7.47% for the <sup>99m</sup>Tc source and 6.24% for the <sup>18</sup>F source, both values located at the lower resolution limit of the measurement system (< 1 MBq). For

activity levels greater than the lower resolution limit of the system, the mean values of the deviations were 0.56 (± 1.79)% for the <sup>99m</sup>Tc source and 0.92 (± 1.19)% for the <sup>18</sup>F source, indicating an excellent quality of the system in the measurement of different activity quantities of a same radioisotope.

The adjustment of an exponential function of the  $y = a + be^{\lambda t}$  and  $\lambda = 0.693/T_{1/2\text{physical}}$  types, for the experimental data for the <sup>99m</sup>Tc and <sup>18</sup>F sources allowed for the calculation of the physical half-life for both elements, whose values were, respectively, 5.949 (± 0.002) hours and 1.816 (± 0.007) hour



**Figure 2.** Characteristic chart of the linearity test performed with the  $^{99m}\text{Tc}$  source, indicating the upper and lower thresholds of acceptable deviations for the purpose of this testing.



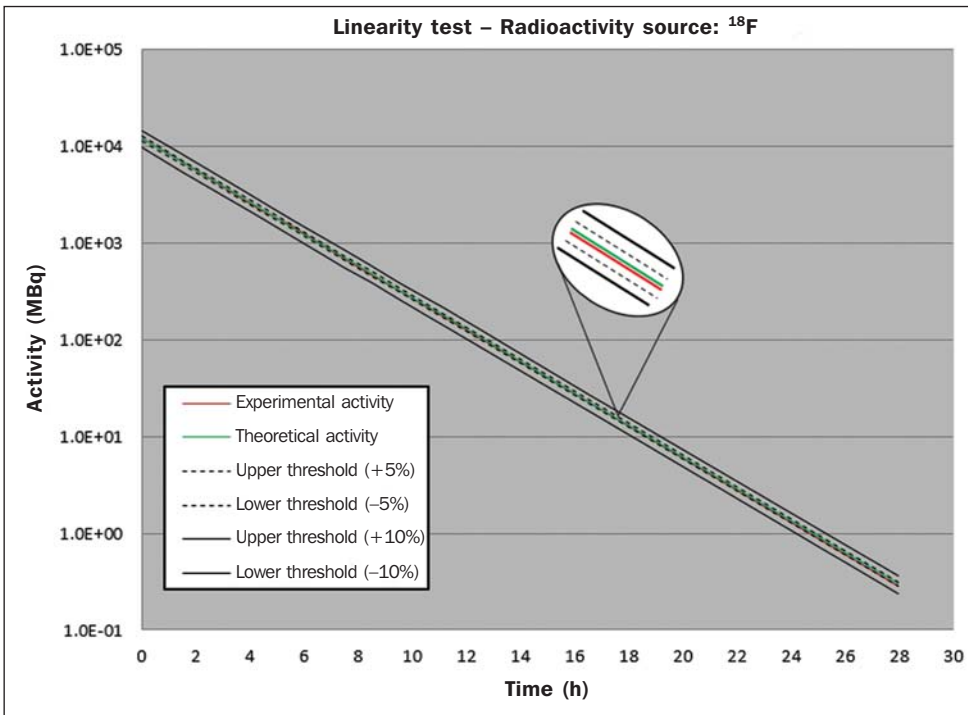
**Figure 3.**  $^{18}\text{F}$  source activity decrease as a function of time as measured in the  $^{18}\text{F}$  and  $^{99m}\text{Tc}$  windows.

with a difference of less than 1% from values reported in the literature<sup>(6)</sup>.

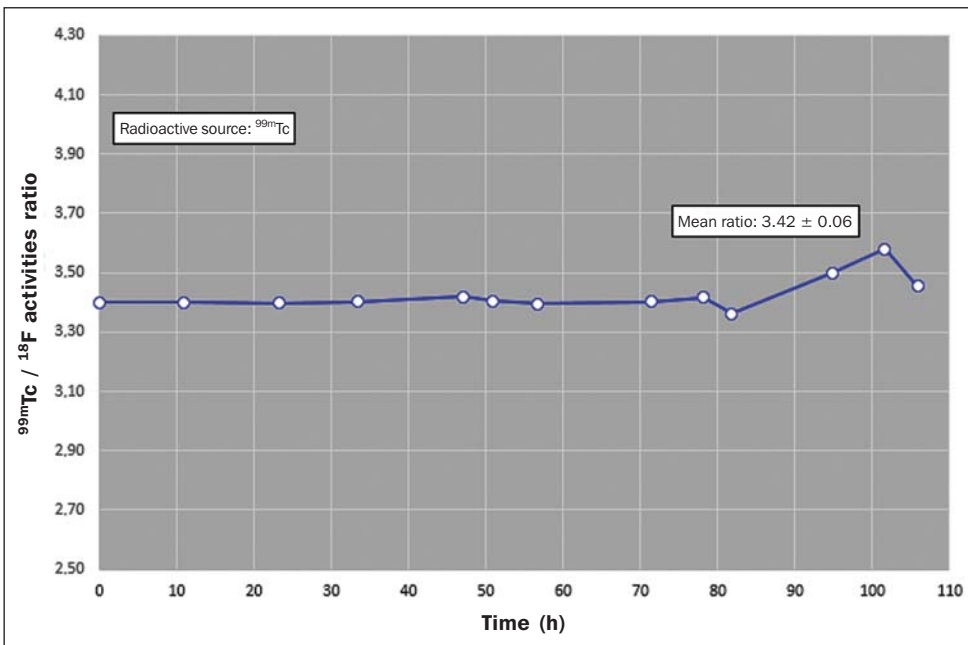
The mean ratio between the activities indicated by the equipment for the  $^{99m}\text{Tc}$  source when measured at the respective  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  windows was  $3.42 (\pm 0.06)$  while for the  $^{18}\text{F}$  source was  $3.39 (\pm 0.05)$ . Such ratios were considered constant throughout the entire measurement period (Table 1) implying the possibility of utilization of both ra-

dioisotopes in the linearity test, independently from the window utilized to measure the source, as the linearity test aims at evaluating the equipment response in the measurement of different activity quantities, whose response should be linear in the interval between the lower and upper limits of activity utilized at the nuclear medicine clinic on a daily basis<sup>(4)</sup>.

As regards costs, the acquisition cost of a  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator with 6.75 GBq (250 mCi) for the performance of



**Figure 4.** Characteristic chart of the linearity test performed with the  $^{18}\text{F}$  source, indicating the upper and lower thresholds of acceptable deviations for the purpose of this testing.



**Figure 5.** Ratio between activity values indicated by the dose calibrator for a  $^{99m}\text{Tc}$  source as measured in the  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  windows.

the linearity test is about R\$ 1,300.00, while a  $^{18}\text{F}$ FDG source with 6.75 GBq (250 mCi) amounts to approximately R\$ 3,500.00, according to a 2014 inquiry to Ipen, an organ of CNEN and main radioisotopes supplier in the Brazilian market.

## DISCUSSION

The electric current generated at an ionization chamber-based dose calibrator, which is proportional to the activity, is related both to the quantity of radioactive atoms existing at a given sample and to the photons energy released

during the disintegration process. The same electric current per activity unit (pA/MBq – picoampere per MBq) may be obtained from different radioisotopes, a fact that hinders the identification of the radioisotope by the dose calibrator during the measurement process. Thus, in order to obtain a reliable reading from the dose calibrator it is necessary to enter correction factors for the electric current proportional to the radioisotope to be measured, and that is automatically obtained by means of the radioisotope selector that exists in the equipment. Generally, the correction factors between a given radioisotope and another are constant, taking as a ref-



erence the radioisotopes utilized by the manufacturer in the initial calibration of the equipment, such as the  $^{60}\text{Co}$  and  $^{137}\text{Cs}$ (<sup>2</sup>) radioisotopes.

Usually, the linearity test provides good results within acceptable parameters, provided the characteristics of the measurement system, such as good precision, accuracy and daily constancy testing are properly maintained. In the present study, the tests were carried out with  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  sources and in both cases the excellent quality of the equipment was independently demonstrated by measuring different activity quantities from radioisotopes with quite distinctive energies, namely 141 keV ( $^{99m}\text{Tc}$ ) and 0.511 MeV ( $^{18}\text{F}$ )(<sup>6</sup>) (Figures 2 and 4).

The practically constant ratio between the activities indicated by the equipment for a same source measured at different windows (Table 1; Figures 5 and 6) allows for the demonstration that the utilization of a single radioisotope, for example,  $^{99m}\text{Tc}$ , could be enough for the performance of the linearity test, independently from the utilization of  $^{18}\text{F}$ , either exclusively or not, by the nuclear medicine clinic. Conceptually, the response from a dose calibrator is considered to be linear whenever the measured response/estimated response ratio or deviation remains constant along time, a fact that was experimentally demonstrated in the present study (Table 1)(<sup>5</sup>).

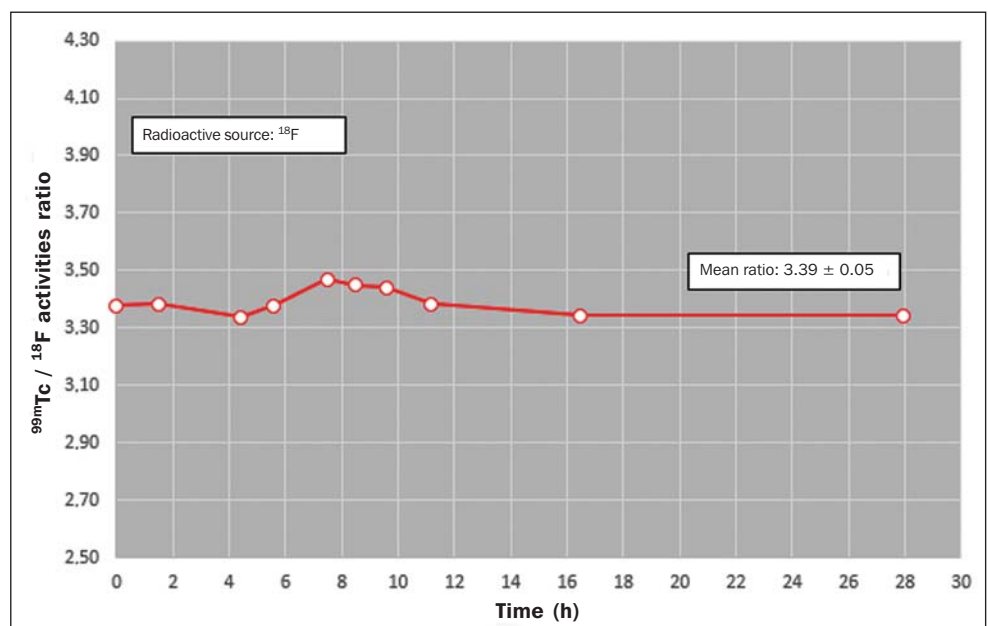
Additionally, the linearity test evaluates the ionization chamber's saturation characteristics, as well as the electrometer linearity in the electric current measurement. Therefore, the linearity test is not directly linked to the utilized radioisotope, but rather to the amount of electrical loads generated during the measurement process. Thus, the linearity test could be performed with different radioisotopes provided the electric current interval, proportional to the activity interval to be tested are within the limits applied at the nuclear medicine clinic. Such information is very important and useful

for those clinics operating exclusively with positron emitters, as is the case of  $^{18}\text{F}$ .

The AAPM Report No. 181(<sup>5</sup>) has indicated that the elements of choice for performance of linearity tests have been  $^{99m}\text{Tc}$  and  $^{18}\text{F}$ , considering that routine tests with all available radioisotopes are not practicable. There is also evidence that there is a lack of consensus on the activities to be utilized in the test, a situation where some entities recommend the performance of tests with activities within the interval where the dose calibrator will be utilized, while others such as IAEA recommend the test to be initiated with the maximum activity administered to the patients in the clinic routine, although all of the entities are in agreement that the minimum activity to be tested should approach the resolution values of the measurement system ( $\sim 1 \text{ MBq}$ )(<sup>5</sup>). However, one should consider the fact that not every measured activity will be administered to patients, such as, for example, the activities that will be stored as liquid radioactive waste and, in this particular case, the correct measurement of the activity is a very important factor impacting the storage time span of such waste.

The difference in costs for the performance of the linearity test either by utilizing  $^{99m}\text{Tc}$  or the  $^{18}\text{F}$  radioisotopes is very significant, reaching a 40% difference between the two radioisotopes.

A viable option for further reduction in costs would be the supply of de  $^{99m}\text{Tc}$  activities by the radioisotope purveyors with the single and exclusive purpose of being utilized for linearity testing. In this context, an inquiry to Ipen for the supply of a 13.5 GBq (500 mCi)  $^{99m}\text{Tc}$  activity resulted in a cost lower than that of a generator, or even free of any cost, depending on favorable logistics, thus sharply impacting the cost of the linearity test. It is also important to emphasize that the utilization of  $^{99m}\text{Tc}$  sources instead of  $^{18}\text{F}$  sources implies a reduction in the potential occupational and



**Figure 6.** Ratio between activity values indicated by the dose calibrator for a  $^{18}\text{F}$  source as measured in the  $^{99m}\text{Tc}$  and  $^{18}\text{F}$  windows.

environmental exposure, as a  $^{18}\text{F}$  source presents a dose potential 10 times higher than that of a  $^{99m}\text{Tc}$  source with the same activity, namely,  $135.1 \mu\text{Gy}/\text{GBq}\cdot\text{m}^2\cdot\text{h}$  and  $14.1 \mu\text{Gy}/\text{GBq}\cdot\text{m}^2\cdot\text{h}$ , respectively<sup>(9)</sup>.

The present study demonstrated the possibility of optimizing dose calibrators linearity testing, drawing the attention of investigators and regulatory agents towards a careful evaluation of the present data, as the dissemination of such information might translate into cost reduction for both private and public health services, without impairing the continuous development of the quality of services rendered to society.

## CONCLUSION

The physical characteristics of the dose calibrator utilized in the present study allow for the indication that the results obtained in the linearity tests with  $^{99m}\text{Tc}$  can be validated for the utilization of  $^{18}\text{F}$ . Such a result extrapolation, presumably extensible to other apparatuses of similar configuration and in satisfactory conditions of utilization, in association with the high exposure potential and acquisition cost of  $^{18}\text{F}$ , suggest that  $^{99m}\text{Tc}$  could be utilized for linearity tests in clinics that utilize  $^{18}\text{F}$ , without impairing the procedure as well as the assurance of the nuclear medicine service quality.

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