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Perfomance analysis of a small animal PET scanner using ^{68}Ga Isotope

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Astract: In recent years, the use of PET scanners for small animals in preclinical research has been growing in Brazil, due to this fact it is essential to have a quality assurance program to ensure the good performance of these scanners or indicate the need for corrective maintenance. In 2008, the National Association of Electrical Equipment Manufacturers (NEMA) in the USA published a document that in your section 6 - Image Quality, Accuracy of attenuation and scatter corrections - proposes the following tests to ensure quality control: uniformity, spill-over ratio, and recovery coefficients. Thus, the objective of this work was to evaluate the performance of a small animal PET scanner *LabPET SOLO 4* using the isotope ^{68}Ga. The results of tests using the ^{68}Ga isotope showed significant differences when compared with the results of tests using ^{18}F. The paper provided us with a comprehensive understanding of the functioning of the PET scanner when employing the radionuclide ^{68}Ga. This evaluation is of crucial relevance for application in laboratories, especially in the quantitative analysis of PET images and in the planning of preclinical studies.

Keywords: ^{68}Ga, Image Quality, Preclinical PET.

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Análise de desempenho de um scanner PET para pequenos animais utilizando o isótopo ^{68}Ga

Resumo: Nos últimos anos, o uso de scanners PET para pequenos animais na pesquisa pré-clínica vem crescendo no Brasil, devido a este fato é imprescindível um programa de garantia de qualidade para garantir o bom desempenho desses scanners ou indicar a necessidade de manutenção corretiva. Em 2008, a Associação Nacional dos Fabricantes de Equipamentos Elétricos (NEMA) nos EUA publicou um documento que em sua seção seis – Qualidade da Imagem, Correção de Atenuação e Correção de Espalhamento - propõe os seguintes testes para garantia do controle da qualidade: uniformidade, razão *spill-over* e coeficientes de recuperação. Dessa forma, o objetivo deste trabalho foi avaliar a qualidade da imagem do PET scanner para pequenos animais LabPET SOLO 4 utilizando o isótopo ^{68}Ga. Os resultados revelaram que o uso do isótopo ^{68}Ga foi bastante diferente dos testes padrão usando ^{18}F. O projeto nos proporcionou uma compreensão abrangente do funcionamento do scanner PET ao empregar o radionuclídeo ^{68}Ga. Essa avaliação detém relevância crucial para a aplicação em laboratórios, sobretudo na análise quantitativa de imagens PET e no planejamento de estudos pré-clínicos.

Palavras-chave: ^{68}Ga, Qualidade da Imagem, PET pré-clínico.

1. INTRODUCTION

In recent years, the use of small animals PET scanners in pre-clinical research has been growing in Brazil. There are currently seven small animals PET scanners spread across research centers across the country [1], demonstrating that this type of scanner is an important tool for non-invasive in vivo studies on animals, which contribute to the development of new medicines and radiopharmaceuticals.

Gallium-68 has gained substantial momentum since 2003 as a versatile radiometal that is extremely useful for application in the development of novel oncology targeting diagnostic radiopharmaceuticals. Nowadays, there are many radiopharmaceuticals prominence in current clinical guidelines like as [68Ga]Ga-PSMA and [68Ga]Ga-FAPi. Therefore, it is necessary to carry out a quality assurance program to ensure the good performance of the small animal PET scanners and to indicate the need for corrective maintenance [2].

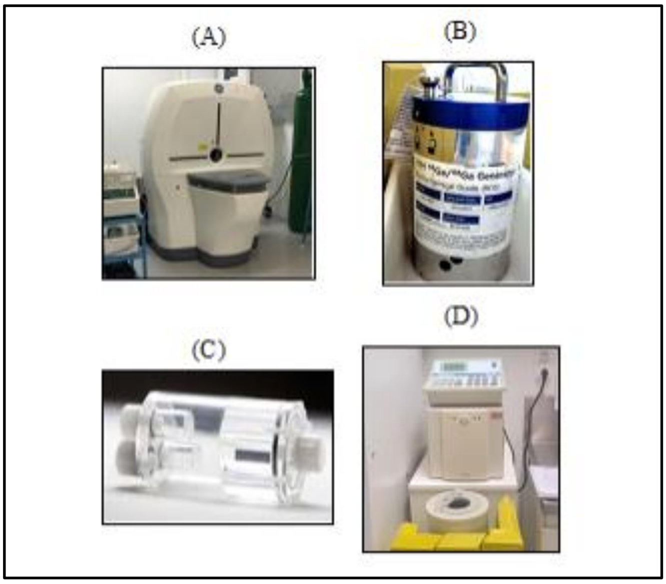
In 2008, the National Electrical Manufacturers Association (NEMA) in USA published a specific document that proposed a standardized methodology for evaluation of the performance of small animal PET scanners [3] – Used not only in USA. Among the parameters covered in Publication NEMA NU 4-2008, three specific parameters are related to Image Quality: (i) uniformity, (ii) spill over ratio and (iii) recovery coefficients. To perform the tests related to these parameters a specific fillable phantomp must be used to acquire the small animal PET image.

The main objective of this work is to evaluate the perfomance of the LabPET SOLO 4 scanner using the ^{68}Ga isotope in this sense, the tests in section 6 of the NEMA NU-4/2008. Knowledge of the PET image quality parameters related to the ^{68}Ga isotope is essential to ensure the appropriate use of this isotope in small animal PET imaging.

2. MATERIALS AND METHODS

During the development of this work, we used the following materials: (i) a small animal PET scanner GE HealthCare LabPET SOLO 4, (ii) a commercial ^{68}Ga/^{68}Ge generator, (iii) a specific NEMA IQ PHANTOM for evaluating Image Quality, (iv) a CAPINTEC CRC 25® activity meter. These materials are presented in Figure 1:

Figure 1: Materials: (A) GE HealthCare LabPET SOLO 4, (B) commercial ^{68}Ga/^{68}Ge generator, (C) specific NEMA IQ PHANTOM (D) CAPINTEC CRC 25® activity meter.



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The phantom is made up of polymethylmethacrylate (PMMA) with internal dimensions of 50 *mm* length and 30 *mm* diameter. It possesses a main chamber that communicates with five different diameters auxiliary rods (1, 2, 3, 4, and 5 *mm*), all of which are expected to be filled with radiopharmaceutical water solution. Thus, activity concentration in any rod is the same that the one in main chamber. In addition, the IQ phantom possess two cold chambers - one of them to be filled with air and the other one with water, both no radioactive [3, 4].

The ^{68}Ga/^{68}Ge generator was luted according to the manufacturer's recommendations [5] using HCL solution, 0.05 M. The $^{68}GaCl_3$ eluate was further diluted with water deionized before filling the IQ PHANTOM. The phantom filled with radioactive aqueous solution (3.62 MBq) was measured using a CAPINTEC CRC 25® activity meter configured according to the manual [6] to correctly measure the nuclide 68Ga. The internal fillable volume of the IQ phantom is 22 *mL*. Thus, the activity concentration in the IQ phantom was 164 kBq.*mL*-1 based to recommendation of NEMA NU 4/2008.

The IQ phantom was placed on the small animal PET scanner imaging bed to simulate a real mouse PET imaging. Table 1 summarizes the experimental conditions for acquisition and reconstruction of the PET images. The protocol used follows the standard used by the Molecular Imaging Laboratory of the Nuclear Technology Development Center and previous work. [7]. Acquisition and reconstruction of PET images were performed with LabPET 1.12.1 software provided by the small animal PET scanner manufacturer [3].

Table 1: Experimental conditions of PET images acquisitions and reconstructions.

Step	Parameter	Value
Acquisition	Acquisition time (min)	20
	Number of bed positions	3
	Acquisition mode	Spatial
	Activity (MBq)	3.62
Reconstruction	FOV (*mm*)	46
	Algorithm	MLEM-3D
	Number of iterations	20
	High resolution mode	No

After image acquired and reconstruction, image quality tests recommended by the NEMA 4-2008 publication [3] were performed following parameters, namely Uniformity, Spill-Over Ratio (SOR) and Recovery Coefficient (RC):

The Uniformity test consists of obtaining mean (ACmean), maximum (ACmax), minimum (ACmin) and standard deviation (ACSD) of the activity concentration in the main chamber. To perform this test, a central cylindrical volume of interest (VOI) with 22.5 *mm* diameter and 10 *mm* height shall be analyzed. The number of counts per second (CPS) in the VOI were converted in activity concentration (kBq.*mL*-1) using a previous calculated conversion factor (CF). The CF was obtained from a VOI positioned on the acquired image of the phantom. Then, the average count rate per voxel unit (cps/voxel) and the number of voxels contained in the VOI were extracted. Thus, the concentration of the count rate per volume (cps/*mL*) was obtained and the activity to count rate ratio (Bq/cps) could be calculated, since the real volume of the phantom and the activity introduced into it were known. The activity concentration percentage standard deviation (%SD), also named image roughness (%IR) [8], was evaluated according to the equation (1):

$$\%SD = \%IR = 100\ X\ \frac{ACsd}{ACmean} \tag{1}$$

where ACSD is the standard deviation of the activity concentration measured in VOI of 22.5 *mm* diameter and 10 *mm* height positioned in the uniform region of the IQ PHANTOM; and ACmean is the mean activity concentration measured in the same VOI.

The ratio between the mean activity measured in a cold chamber (filled with air or water) and the mean activity measured in the main chamber provides the Spill-Over Ratio. To perform this test, a central cylindrical VOI (4 *mm* diameter, 7.5 *mm* heigh) shall be analyzed.

The ratios between the mean activity measured in each one of the five auxiliary rods and the mean activity measured in the main chamber provides the image Recovery Coefficients. To perform this test, the 10 *mm* length central region of each rod shall be average to obtain a single image in which the coordinates of the highest value pixel are determined. Then, for each rod, the mean activity concentration must be determined considering a 10 *mm* axial line passing through the highest value pixel.

3. RESULTS AND DISCUSSIONS

Figure 2 shows the ^{68}Ga PET image of the IQ phantom, in different sections. Figure 3 shows the VOIS positioned in the image for the tests according to the NEMA NU 4-2008 publication.

Figure 2: ^{68}Ga-PET image of the IQ phantom. A: transverse section passing through the IQ PHANTOM main camera. B: transverse section passing through the region of the cold chambers. C: transverse section passing through the region of the auxiliary rods.

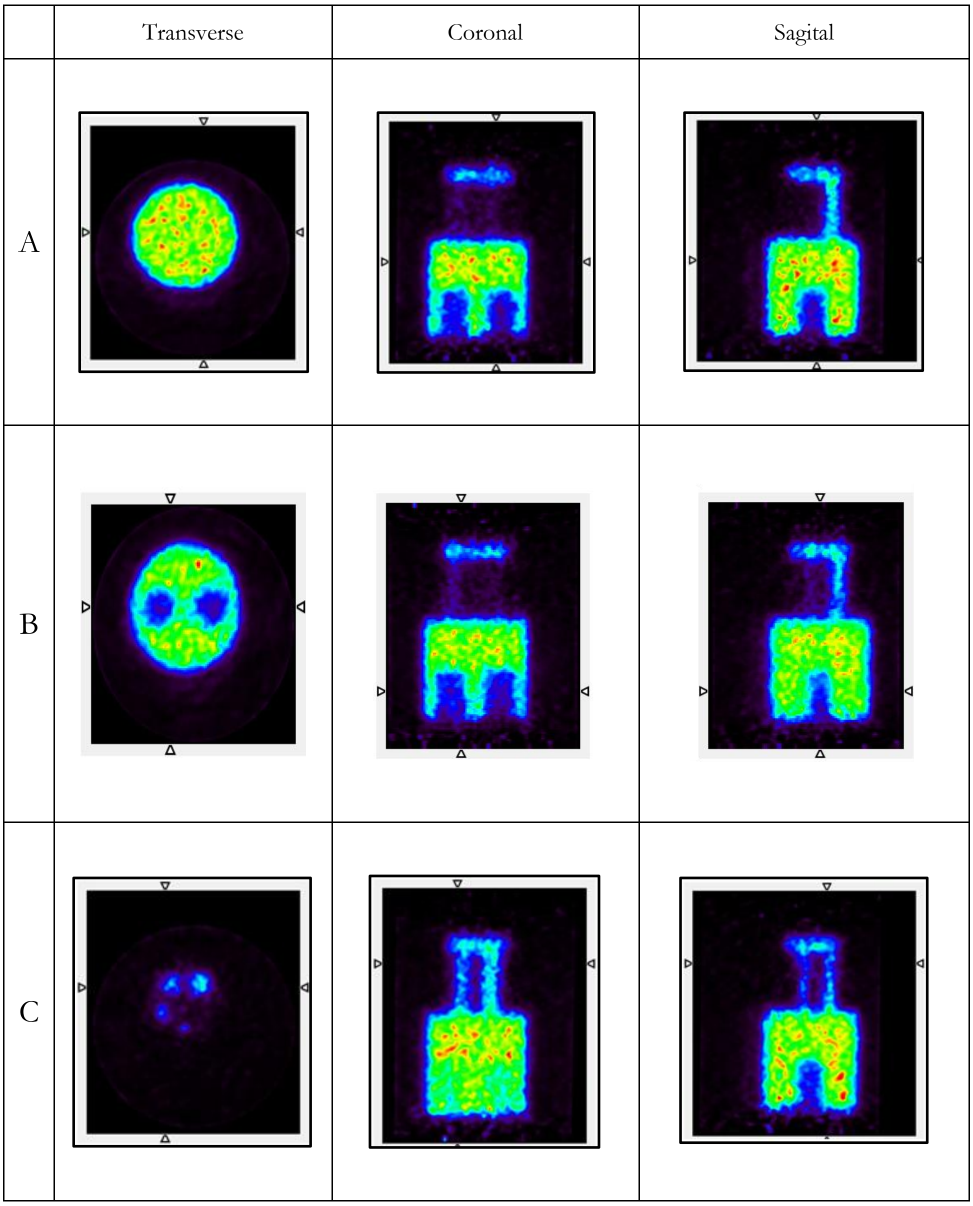

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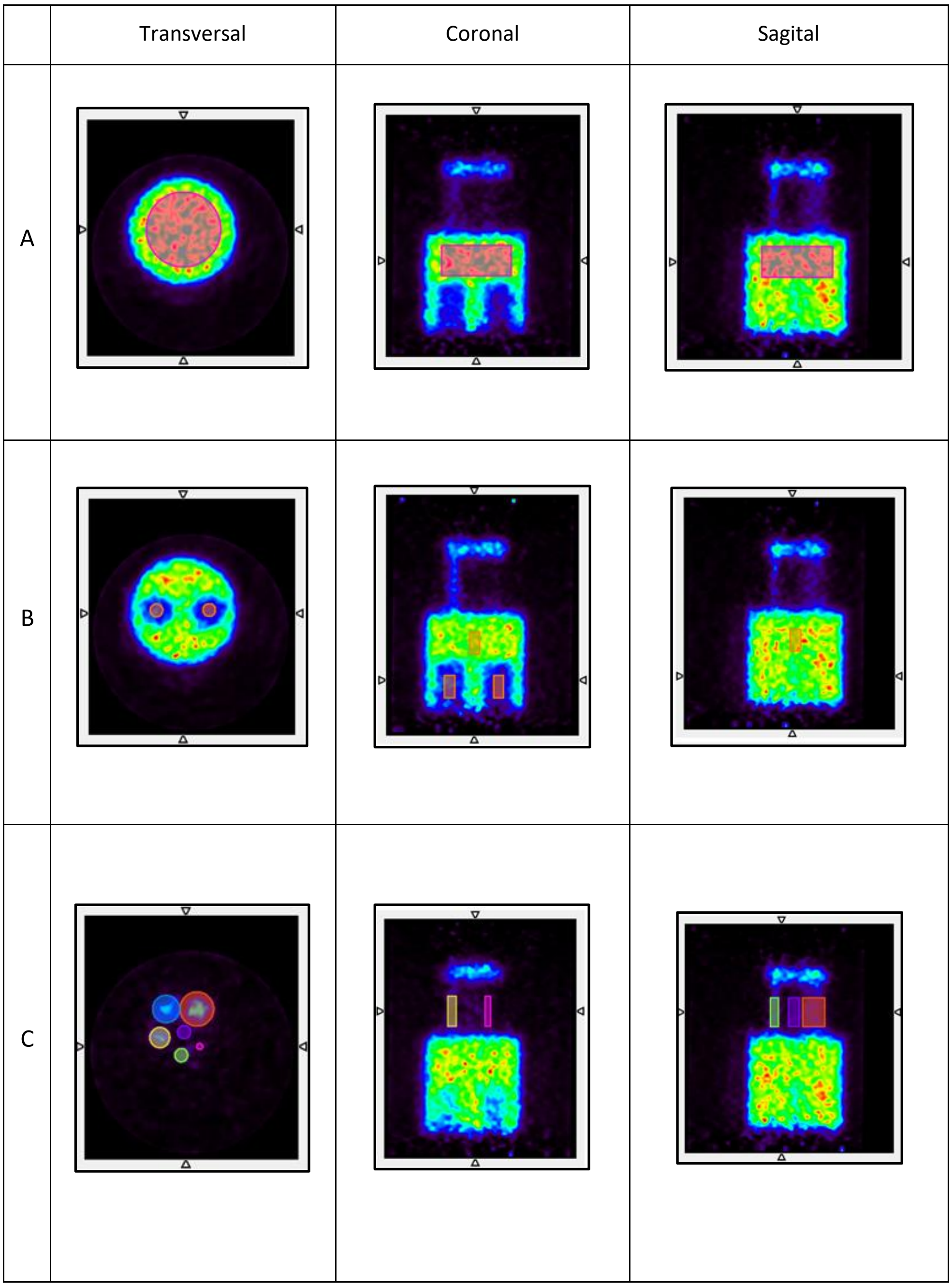
Figure 3: VOIs positioned to perform the tests. (A) VOI for the Uniformity test, (B) VOIs for the Spillover Ratio test, (C) VOIs for the Recovery Coefficients test.



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The results obtained in the tests for image quality evaluation are represented in Table 2.

Table 2: Test results for: Uniformity, Spillover Ratio and recovery coefficient.

Uniformity Test				
Mean	**SD**	**Minimum**	**Maximum**	**%SD**
192.59	24.51	357.13	891.82	13

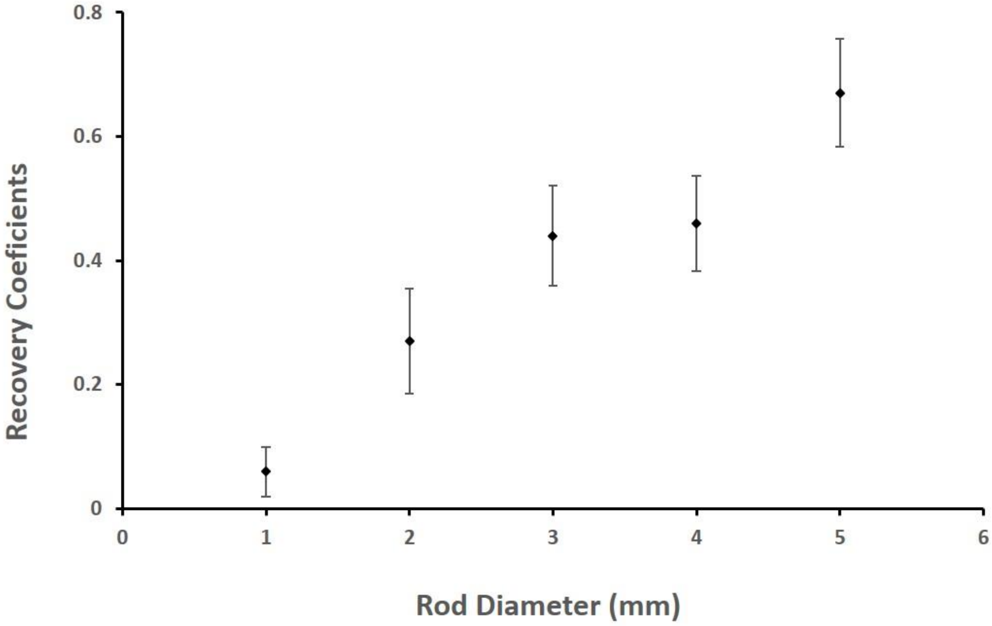
Spillover Ratio Test	
Water	**Air**
0.20 ± 20%	0.29± 26%

The results indicate a roughness of 12.73%. Previous studies using ^{18}F indicated an image roughness of 8% [7]. This difference was already expected due to the penetration range of the ^{68}Ga positron being greater in relation to the ^{18}F positron. Positron penetration generates an error in the true location of the positron emission, the site of annihilation. Additionally, it was observed that the average value of activity concentration obtained in the uniformity test was 193 ± 25 kBq.*mL*-1, compatible with the nominal value injected into the phantom of 164 kBq.*mL*-1.

In the Spill-over Ratio (SOR) test, the values obtained are close to the results found in previous studies, which used 17 images with ^{18}F [7]. For water, the SOR of ^{68}Ga was 0.20 ± 20% and with ^{18}F the values range from 0.15 to 0.22 with an average of 0.18 ± 0.02. For air, the SOR is 0.29 ± 26% and with ^{18}F the values vary from 0.25 to 0.33 with an average of 0.28 ± 0.02. It is important to note that although the average values are similar, in the study with ^{68}Ga the standard deviations are much greater than in the study with ^{18}F. Such an observation can again be explained by the difference in the range of the positrons.

Figure 4 presents recovery coefficients results. In this test, the values found are worse than the results found for ^{18}F [4]. For a 5 mm rod (^{18}F: 0.89; ^{68}Ga: 0.67) and for a 1 *mm* rod (^{18}F: 0.10; ^{68}Ga: 0.06), the values found show the difference in performance between the isotopes. These results were expected considering the difference of range positron (mean range in water for fluorine is 0.6 *mm* and 3.5 *mm* for gallium) [12]. The RC parameter affects image quantification and visualization of small structures and low/high uptake interfaces.

Figure 4: Recovery Coefficients test.



4. CONCLUSIONS

Results reveal that using the ^{68}Ga isotope were quite different from the standard tests using ^{18}F. These results were expected, since the difference in the range of the ^{68}Ga positron is greater than the range of the ^{18}F positron, increasing the probability of the equipment making an erroneous reading of the true location of the positron emission. Thus, the work allowed us to understand the performance of the PET scanner when using the ^{68}Ga radionuclide. This evaluation is important for practice in laboratories, especially for the quantitative analysis of PET images and in the planning of preclinical studies.

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