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Comparative analysis of image quality parameters and qualitative spatial resolution of three small animal PET scanners in Brazil

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ABSTRACT

This study evaluated Image Quality (IQ) parameters and qualitative spatial resolution (SR) of Triumph® LabPET systems installed in three different Brazilian preclinical molecular imaging centers. A comprehensive evaluation of the PET scanner intrinsic parameters is important to optimize the acquired images, providing more reliable qualitative and quantitative analyses. Experiments were carried out at the centers: C1 at CDTN/CNEN; C2 at HCFMUSP; C3 at PUC-RS. IQ phantom PET images were acquired as recommended in NEMA NU 4-2008 standard. Image reconstructions were performed in each system using the same reconstruction protocol. Data was processed using PMOD® software. The IQ parameters: (i) uniformity, (ii) spill-over ratio (SOR) and (iii) recovery coefficients (RC) were evaluated and compared. For Uniformity test, the percentage standard deviations of mean activity concentration were 7.8%, 7.3% and 6.4% for Centers 1, 2 and 3 respectively. Cold chambers SOR values in the systems 1, 2 and 3 were respectively 0.16, 0.19 and 0.21 for water; 0.26; 0.28 and 0.30 for air. The RC's for rod diameters from 1 to 5 mm ranged from 0.08 to 0.91 for the three centers. The qualitative SR is in the limit of 1.2 mm. Results revealed that the three PET systems have appropriate quality parameters for preclinical studies, presenting values compatible with international standards. This study was able to reveals the performance of preclinical PET system of different Brazilian imaging centers and may support the standardization of a National Quality Control Program for Small Animal PET scanners.

Keywords: **image quality; preclinical PET scanner; NEMA NU 4-2008.**

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1. INTRODUCTION

Positron Emission Tomography (PET) is an important molecular imaging technology and is widely used in preclinical studies, generating static and dynamic images applied to biochemical, metabolic and functional study of organs and tissues of small animals. Most of molecular imaging research is undertaken in small animals (e.g, preclinical PET scanner imaging) which provide a bridge between *in vitro* studies and human clinical imaging. Thus, PET for small animals can be considered a translational research tool between animal models and human clinical applications [1].

Currently in Brazil, there are six centers of preclinical molecular imaging using seven PET systems routinely for the development of new radiopharmaceuticals or in studies of new applications of traditional radiopharmaceuticals [2]. Therefore, every imaging technology needs to be evaluated by a set of quality tests that confirms their performance or indicates the need for corrective maintenance [3].

The National Electrical Manufactures Association (NEMA) in USA published its NU 4-2008 standards, a consistent set of methodologies for measuring scanner performance parameters for small animal PET imaging [4]. On the other hand, in Brazil, there is no specific legislation that requires quality tests for PET imaging system or activimeters in preclinical imaging laboratories. National regulatory agencies do not yet have a publication to establish in detail all necessary tests for preclinical equipment. In addition, there is a lack of knowledge for some methodological aspects of small animals PET scanner [5].

In this context, this work aimed to evaluate Image Quality (IQ) parameters and Spatial Resolution of LabPET^{TM} systems installed in three different Brazilian preclinical molecular imaging centers - which corresponds to half of the centers installed in the country [6].

2. MATERIALS AND METHODS

The experiments were carried out in three different centers of preclinical molecular imaging in Brazil presented in Table 1. Additional collaboration of the radiopharmaceutical production on site made the ^{18}F-FDG sources available.

Table 1: Brazilian centers of preclinical molecular imaging covered in this study.

#	Center	Institution	Federal Unit	Region
I	Molecular Imaging Laboratory (LIM)	CDTN/CNEN	MG	Southeast
II	Nuclear Medicine Laboratory (LIM-43)	HCFMUSP	SP	
III	Laboratory of Bioimaging Preclinical Research Center (CPPC)	BraIns PUC-RS	RS	South

Note: CDTN: Centro de Desenvolvimento da Tecnologia Nuclear; CNEN: Comissão Nacional de Energia Nuclear; MG: Minas Gerais, HCFMUSP: Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo; SP: São Paulo, BRAINS PUC-RS: Instituto do Cérebro - Pontifícia Universidade Católica do Rio Grande do Sul.

2.1 PET scanners

The LabPET™ is a digital PET scanner which uses scintillation crystals and avalanche photodiodes (APDs) as detectors [7, 8]. Two different types of scintillators are used, $Lu_{0.4}Gd_{1.6}SiO_5$ and $Lu_{1.9}Y_{0.1}SiO_5$ (LGSO/LYSO), and the scanner possess a stationary gantry. LabPET images are acquired using a 250-650 keV energy window and 22 ns coincidence timing window and the scanner can operate in a dynamic or static mode [9, 10]. Coincidence data is saved in a list mode and can be sorted out as sinograms.

In Brazil, two versions of the LabPET™ scanner are installed in molecular imaging centers: LabPET 4 and LabPET 8. Some important characteristics and features of LabPET 4 and LabPET 8 are summarized in Table 2. More details about the LabPET™ design and architecture are presented elsewhere [11, 12].

Table 2: LabPET 4 and LabPET 8 technical specifications [8]

Parameter	Specification	
	LabPET 4™	LabPET 8™
Scintillation Crystals	Phoswich pair of LYSO and LGSO	
Crystal Dimension	2.0 x 2.0 x 12/14 mm^3 (LYSO/LGSO)	
Number of Crystals	3072	6144
Axial field-of-view (cm)	3.75	7.5 mm
Transaxial field-of-view (cm)	10	10

Table 3 presents the small animals PET scanners characterized in this study and Figure 1 presents an overview of the respective centers of preclinical molecular imaging.

Table 3: Preclinical PET systems characterized in this study

	PET system
I	LabPET Solo 4
II	LabPET 8 - Trimodality (SPECT/PET/CT)
III	LabPET 4 - Bimodality (PET/CT)

Figure 1: LabPET systems in the centers of preclinical molecular imaging

I

II

III

2.2 Spatial Resolution Evaluation

A qualitative analysis (visual inspection) of the Spatial Resolution of the preclinical PET systems was performed using the *HotRod* Phantom. The QRM Micro-PET *HotRod* phantom (Figure 2) consists of 3 cylinders: 2 compacts and 1 containing 6 sets of grouped fillable rods with different diameters (0.6; 0.8; 1.0; 1.2; 1.5; 2.0mm) [13].

Figure 2: (A) HotRod Phantom; (B) internal cylinders; (C) schematic picture of the rods.

(A) (B) (C)

Source: Authors Archive.

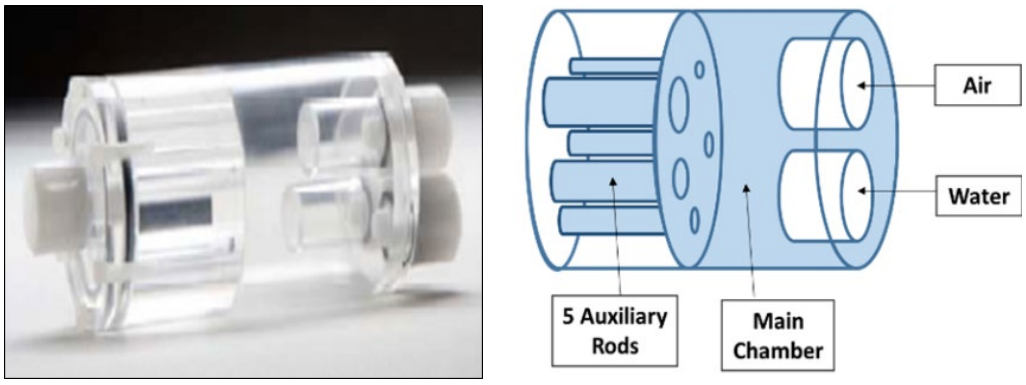
PET images of *HotRod* phantom were acquired using 60 MBq of ^{18}F-FDG for one hour [14]. This activity value is commonly used in rats for whole-body image acquisition and is below of maximum peak of true coincident events for LabPET platform [15]. PET images were reconstructed using a standardized protocol: iterative algorithm MLEM-3D (Maximum-Likelihood Expectation Maximization); 20 iterations; standard mode resolution [16]. Image data was post-processed using PMOD® software.

2.3 Image Quality Evaluation

The purpose of the IQ test is simulating images of whole-body study of a small animal. For this purpose, the NEMA NU 4-2008 publication [4] recommends the use of a specially designed image quality (IQ) phantom made up of polymethylmethacrylate (PMMA) with internal dimensions of 50 mm long and 30 mm diameter. This phantom consists of three regions: a main hot region, a

cold chamber region made of two cylinders of 15 mm in length and 8 mm diameter filled with air and water, and a hot region consisting of five auxiliary rods with diameters ranging from 1 to 5 mm and 20 mm long (Figure 3).

Figure 3: *(A) IQ Phantom; (B) IQ Phantom Schematic View*



(A) (B)

Source: Gontijo et al., 2022.

The IQ phantom is used to analyze three distinct image quality parameters:

(i) Uniformity (percentage of standard deviation (%SD) of the activity concentration): indicator of the system signal to noise ratio.

(ii) Spillover Ratio (SOR) in each (air and water) cold region: indicator of the system scattering correction performance.

(iii) Recovery Coefficients (RC): indicators of the system spatial resolution.

Image acquisition procedure followed the recommendations of NEMA NU 4-2008 publication (3.7 MBq of ^{18}F-FDG at the beginning of acquisition; 20 min acquisition time). PET images were reconstructed following the LIM/CDTN/CNEN standard protocol [15]: MLEM-3D algorithm; 20 iterations; standard mode resolution; no attenuation or scatter corrections; no post-filtering. PMOD® software was used to perform images post-processing following NEMA NU 4-2008 recommendations while the statistical analysis and graphics results were performed using Excel software.

2.3.1 PET Image Analysis

After image reconstruction, image quality analysis also followed the NEMA 4-2008 publication [4]. A brief description of the analysis of each parameter is presented below:

- Uniformity: This test consists of to obtain mean (AC_{mean}), maximum (AC_{max}), minimum (AC_{min}) and standard deviation (AC_{SD}) of the activity concentration in the main chamber (Figure 3.B). To perform this, 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 was converted in activity concentration ($kBq \cdot ml^{-1}$) using a previous determined conversion coefficient (CC). The percentage standard deviation (%SD) was calculated dividing the standard deviation (AC_{SD}) of the activity concentration by the mean activity concentration and after that multiplying per one hundred.

- Spillover Ratio (SOR): The ratio between the mean activity concentration measured in a cold chamber (filled with air or water) and the mean activity concentration measured in the main chamber provides the Spill-Over Ratio. To perform this, a central cylindrical VOI (4 mm diameter, 7.5 mm height) shall be analyzed. The number of counts per second (CPS) in each VOI (main chamber and cold chamber) is used to obtain the spillover ratio.

- Recovery Coefficient (RC): The ratios between the mean activity concentration measured in each one of the five auxiliary rods and the mean activity concentration measured in the main chamber provides the image Recovery Coefficients. To perform this, 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.

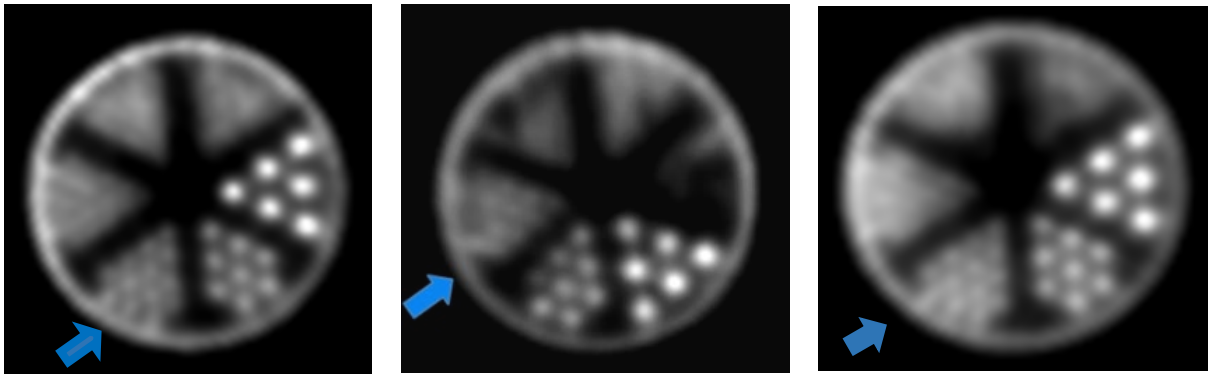
After PET images analyses, results from the three PET scanners were compared. More details of methodology of PET image analysis were presented elsewhere [2; 4].

3. RESULTS AND DISCUSSION

3.1 Spatial Resolution

Figure 4 presents PET images of the *HotRod* phantom. A qualitative analysis of the images indicates that the SR of the systems is in the limit of 1.2 mm rods (Figure 4). Rods of 2.0, 1.5 and 1.2 mm could be visually distinguished.

Figure 4: Spatial Resolution of the PET images



(I) **(II)** **(III)**

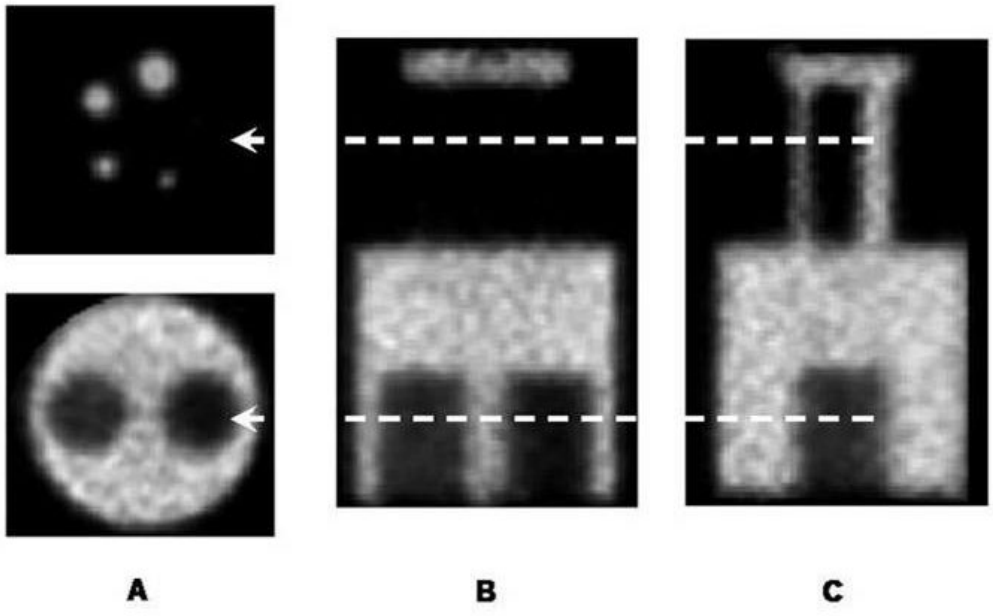
Note: The blue arrows indicate group 3 whose rod diameter is 1.2 mm

It is important to note that results for qualitative SR of PET I agree with previous quality results from Souza *et al*, 2021 [14], which made both analysis qualitative and quantitative of SR - the first with the same method of the present study and the other using a Na-22 point source following NEMA recommendations [4].

3.2 Image Quality

Figure 5 presents a typical PET image of the IQ phantom obtained in this study.

Figure 5: Typical PET image in (A) axial, (B) coronal and (C) sagittal planes of the NEMA IQ phantom.



3.2.1 Uniformity

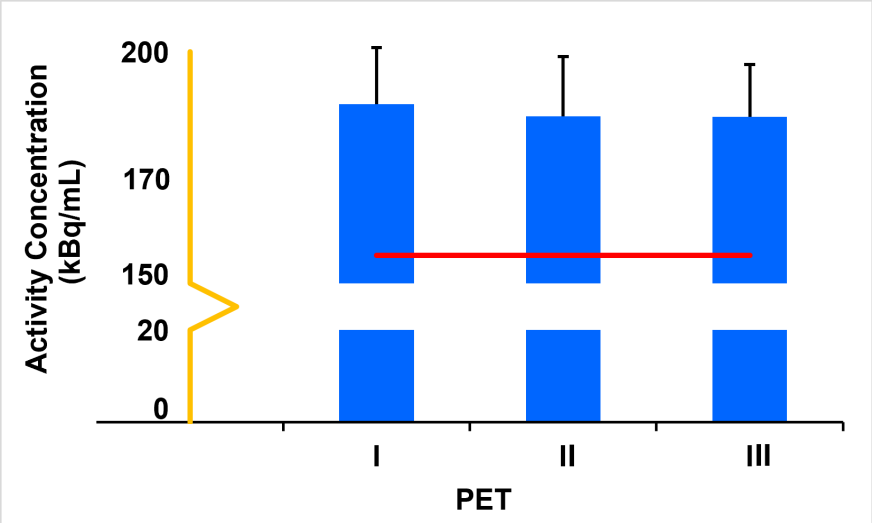
The mean, maximum, minimum and the percentage standard deviation of activity concentration are presented in Table 4. Figure 6 represents the mean of activity concentration and respective errors of all PET scanners and red line is the injected activity concentration.

Table 4: Activity concentration values and percentage standard deviation for each image

PET	AC_{mean}	AC_{SD}	AC_{min}	AC_{max}	%STD
I	179,7	14,6	121,5	246,6	8,1
II	177,1	12,9	135,7	234,5	7,3
III	177,0	11,3	141,5	227,1	6,4

AC = Activity Concentration at main chamber ($kBq \cdot ml^{-1}$);
min = minimum; max = maximum; %STD = Percentage Standard Deviation

Figure 6: Uniformity test results for the preclinical PET scanners.



All activity concentration mean values are higher (5-7%) than expected activity concentration in the IQ phantom ($168\ kBq \cdot ml^{-1}$). It is believed that the conversion coefficient (CC) used to convert (CPS · voxel^{-1}) in ($kBq \cdot ml^{-1}$) was responsible for this systematic overestimation.

Considering that the phantom used to CC determination is smaller than IQ phantom and that the software does not correct scattering, a possible explanation for the finding would be the counting of more scattered events as true events in the IQ phantom when compared to the phantom used for CC determination. More studies are being conducted to clarify this point definitively.

Values of %STD (6.4 – 8.1%) reported by uniformity test in this comparative study (Table 3) were compatibles with 7.0% reported for the LabPET 8 scanner [17]. PET III showed the lowest value, followed by PET II and I. These findings are crucial for researchers at the time of image analysis since upper uptake could be interpretated as a false positive in metabolic images. The researcher's experience and previous knowledge of the biodistribution of the radiopharmaceutical used contribute to the association of preclinical data with image findings, minimizing interpretation mistakes.

3.2.2 Spillover Ratio

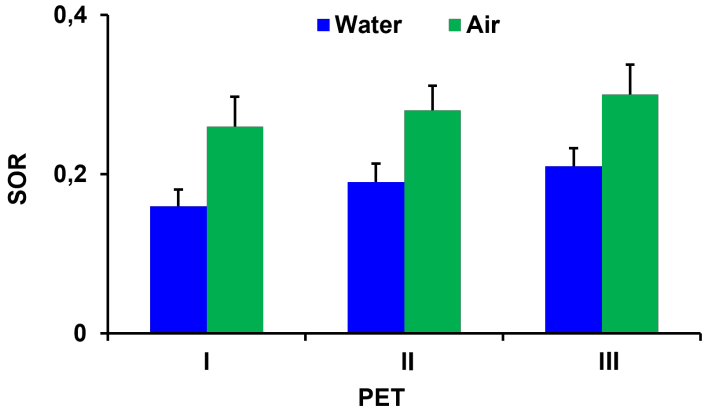
Spillover Ratios (SOR) and the respective percentage standard deviations obtained for the cold chambers (water and air-filled) are reported in Table 5 and compared in Figure 7.

Table 5: Spillover Ratio Test results

#	Region	SOR	%STD	Region	SOR	%STD
I		0.17	18.9		0.26	17.8
II	Water-filled	0.19	12.4	Air-filed	0.28	11.2
III		0.21	10.9		0.30	12.5

%STD = Percentage Standard Deviation

Figure 7: Spillover ratios results for the preclinical PET scanners



The SOR is an indication of the performance of system for the scatter correction. SOR values obtained for the cold chamber filled with water are compatible with the value reported by Prasad *et al*. (2011) for the model LabPET 8 (Water SOR: 0.20) [17]. However, the SOR values obtained for the cold chamber filled with air (Air SOR: 0.26; 0.28 and 0.30, respectively PET I, II and III) are significantly higher than those reported previously (Air: 0.11) [17]. This fact may be explained by different characteristics between the models PET scanners. Both LabPET models (4 and 8) used in this work are not able to perform corrections for attenuation and scatter while the model LabPET 8 used in comparative study performs both corrections.

3.2.3 Recovery Coefficient

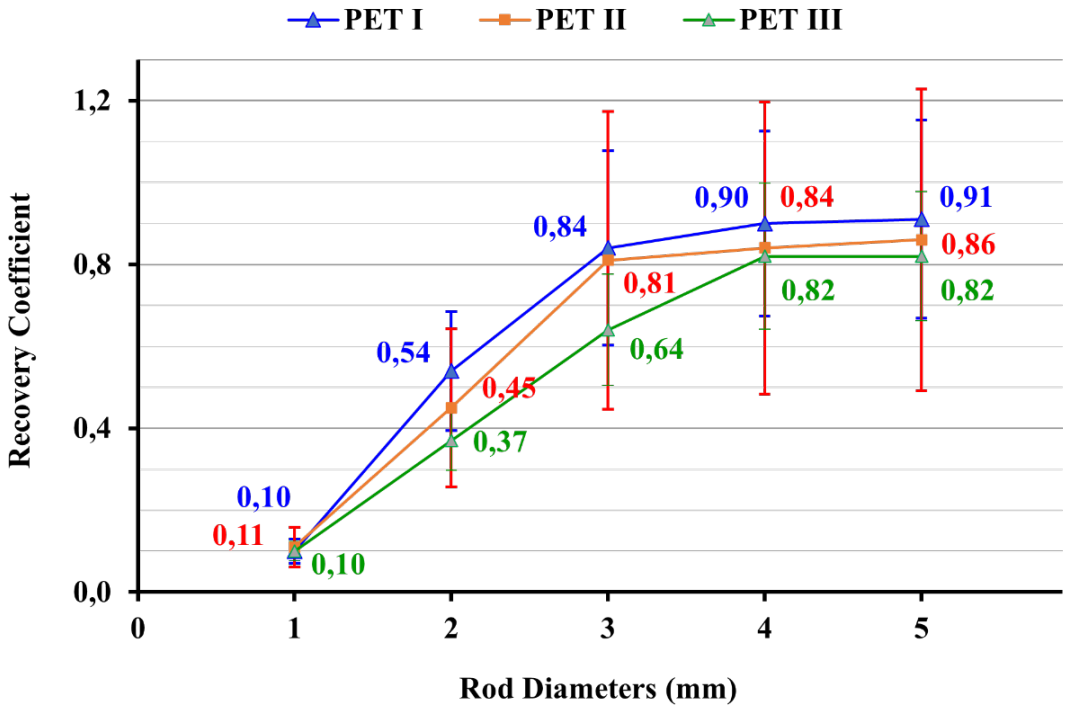
Recovery Coefficients (RCs) and respective percentage standard deviations are shown in Table 6 and comparison of them are represented in Figure 8.

Table 6: Recovery Coefficient Test results

#	1 mm	%STD	2 mm	%STD	3 mm	%STD	4 mm	%STD	5 mm	%STD
I	0.10	29.9	0.54	26.9	0.84	28.2	0.90	25.1	0.90	25.1
II	0.11	44.1	0.45	42.9	0.81	44.9	0.84	42.4	0.86	42.8
III	0.10	23.7	0.37	19.6	0.64	21.2	0.82	21.8	0.82	19.2

mm = milimeter; %STD = Percentage Standard Deviation

Figure 8: Recovery Coefficients for the preclinical PET scanners



The RC values for the five distinct rods varied from 0.10 to 0.91; 0.11 to 0.86 and 0.10 to 0.82 for three PET scanners evaluated respectively. These results demonstrate similar behavior in the 1mm to 5mm cylinders between the different PET scanners. These values are very similar to those previously reported from periodic evaluations for PET I (0.11 to 0.89) [18] and in an international study [17] concerning a LabPET 8 system (0.13 to 0.96).

All PET images were obtained using the same IQ phantom, by the same operator, and using same acquisition and reconstruction parameters. However, in general, RC from PET III presented a

slightly lower performance when compared to the others. It is important to point out that this study is an initial step aiming to know the three PET systems performance. In this step, a single measurement was performed in each PET scanner. So, more measurements in the near future, will permit to evaluate with statistical significance the slightly variability observed in the present paper.

In this context, it is important to note that a greater number of measurements for each PET scanner is necessary to better know the behavior of the PET scanners. However, unfortunately, regulatory agencies in Brazil do not yet have any regulation to establish performance tests and respective periodicity for preclinical PET scanners.

4. CONCLUSIONS

In general, the results demonstrate that all the three small animal PET scanners produce images and is well suited for preclinical molecular imaging research when compared with international literature results that use similar systems [07, 08; 17].

Despite of the results showed that preclinical PET systems evaluated have reliable quality parameters and high-quality images, it is essential to carry out routinely quality control procedures to ensure the reliability and continuous stability of the PET scanner´s quality parameters. The group of authors intends to perform intercomparisons between the preclinical PET scanners of the different Brazilian centers. To this end, the authors proposed a national standardization [19] that was called of Brazilian National Program for Quality Control in the small animal PET scanners.

Summarizing, the analysis of quality parameters is important for all image studies carried out, especially for preclinical PET molecular imaging, particularly those that include quantitative assessments. Therefore, this study was able to reveals characterization of image quality parameters and spatial resolution in three preclinical molecular imaging centers of different regions in Brazil.

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