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Spatial Resolution of a small animal PET scanner using ^{68}Ga isotope

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Abstract: Nuclear Medicine is a modality that has been growing a lot in Brazil and in the world, bringing new radiopharmaceuticals and technologies for the diagnosis and treatment of diseases, making them more effective and accurate. In the development of new radiopharmaceuticals for use in positron emission tomography (PET), the preclinical studies step largely uses PET scanners dedicated to small animals. To achieve this, quality control tests must be carried out to ensure the efficiency of the equipment. Thus, this work aimed to evaluate the spatial resolution of the small animals PET scanner of the CDTN using the isotope ^{68}Ga. In this sense, a microPET hot rod phantom and a commercial ^{68}Ge/^{68}Ga generator were used to obtain PET images. The analysis of the ^{68}Ga-PET images of the simulator was carried out qualitatively and quantitatively and revealed that the spatial resolution of the system using the ^{68}Ga is 3.5 mm.

Keywords: Positron Emission Tomography, PET, Quality Control, Spatial Resolution, ^{68}Ga.

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Resolução espacial de um tomógrafo PET de pequenos animais usando o isótopo ^{68}Ga

Resumo: A Medicina Nuclear é uma modalidade que vem crescendo muito no Brasil e no mundo, trazendo novos radiofármacos e tecnologias para o diagnóstico e tratamento de doenças, tornando-os mais eficazes e precisos. No desenvolvimento de novos radiofármacos para uso em tomografia por emissão de pósitrons (PET), a etapa de estudos pré-clínicos utiliza amplamente tomógafos PET dedicados a pequenos animais. Para isso, devem ser realizados testes de controle de qualidade para garantir a eficiência do equipamento. Assim, este trabalho teve como objetivo avaliar a resolução espacial do tomógrafo PET de pequenos animais do CDTN utilizando o isótopo ^{68}Ga. Nesse sentido, um simulador hot rod microPET e um gerador comercial ^{68}Ge/^{68}Ga foram utilizados para obtenção de imagens PET. A análise das imagens ^{68}Ga-PET do simulador foi realizada qualitativa e quantitativamente e revelou que a resolução espacial do sistema utilizando o ^{68}Ga é de 3,5 mm.

Palavras-chave: Tomografia por emissão de pósitron, PET, Controle de Qualidade, Resolução Espacial, ^{68}Ga.

1. INTRODUCTION

Nuclear Medicine is a modality that has been growing a lot in Brazil and around the world, bringing new radiopharmaceuticals and technologies for the diagnosis and treatment of diseases, making them more effective and accurate.

Currently in Brazil, there are 460 Nuclear Medicine facilities licensed [1]. The main supplier of radiopharmaceuticals in the country is the Nuclear Energy National Commission (CNEN). In 2022, CNEN has made radiopharmaceuticals available for about 2 million medical exams, performed in oncology, cardiology, neurology, endocrinology, nephrology, among other areas of medicine [2]

In the development of new radiopharmaceuticals for use in positron emission tomography (PET), the preclinical studies step largely uses PET scanners dedicated to small animals. Currently in Brazil, there are seven preclinical PET equipment distributed in research centers in the South and Southeast regions of the country [3]. In this context, it is essential that quality control tests are carried out on these devices to determine their performance and ensure the reliability of the study results. Among the various parameters that must be analyzed in quality control tests, one of them is the spatial resolution. Spatial resolution is a measure of the equipment's ability to faithfully reproduce the image of an object, i.e., it is determined as the minimum distance between two points in an image, which influences the quality of the PET image [4].

This work aimed to evaluate the spatial resolution of the small animal PET scanner at the Nuclear Technology Development Center (CDTN) using the ^{68}Ga isotope. CDTN is an institution for research, development, production, services and teaching in the nuclear area and related areas. It is one of CNEN's five nuclear research institutes [5].

Our group has been working with radiopharmaceuticals labeled with ^{18}F and ^{11}C isotopes and now intends to begin studies with radiopharmaceuticals labeled ^{68}Ga. Therefore, knowing the performance of the equipment with the ^{68}Ga isotope is fundamental for the development of future works.

2. MATERIALS AND METHODS

2.1. Materials

In the development of this work, we used (i) a small animals PET scanner, (ii) a simulator dedicated to quality control tests of the small animals PET scanner and (iii) a commercial $^{68}Ge/^{68}Ga$ generator, detailed as follows:

Small Animals PET Scanner

This scanner - model Triumph™ LabPET Solo 4, manufactured by Gamma Medica/GE Healthcare - The LabPET 4 system consists of a stationary portal and employs 1536 detection channels composed of two different types of scintillators, LYSO – Lutetium Orthosilicate with Yttrium (Lu1 .9Y0.1SiO5) and LGSO – Lutetium Orthosilicate with Gadolinium (Lu0.4Gd1.6SiO5), optically coupled to Avalanche Photo Diode (APD) detectors [6]. The detector array is assembled in eight continuous rings in a diameter of 15.6 cm and an axial field of view (FOV) of 3.7 cm. PET images are acquired using an energy window in the range of 250-650 keV and coincidence events with a time window of 22 ns. The system can operate in dynamic or static model.

The equipment is in the Molecular Imaging Laboratory (LIM) of the CDTN. It is routinely used in preclinical studies to acquire metabolic and functional images of organs and tissues of small animals using radiopharmaceuticals produced in the CDTN.

Simulator: QMR MicroPET Hot Rod Phantom

The commercial simulator MicroPET Hot Rod Phantom (QMR manufacturer), shown in Figure 1, is a device made of PMMA, polymethylmethacrylate, specially designed to evaluate the spatial resolution of small animal PET scanners [7]. The simulator has a height of 7 cm, a diameter of 3.5 cm and a volume of approximately 26 cm3. Its interior contains three discs, one of which can be filled. This disc presents fillable channels grouped into six groups with variable diameters, described in Table 1.

Figure 1: QMR MicroPET Hot Rod Phantom Simulator.

(A) (B) (C)

Simulator assembled; (B) Parts of the simulator; (C) Disc with fillable channels

Table 1: Fillable Channels in the Simulator

Group	Channel Diameter (mm)	Channel Spacing (mm)
G1	2.0	4.0
G2	1.5	3.0
G3	1.2	2.4
G4	1.0	2.0
G5	0.8	1.6
G6	0.6	1.2

In the development of this work, the simulator was used to obtain PET images after being filled with a solution of ^{68}Gallium Chloride (^{68}GaCl3, ~5MBq/ml), obtained in the elution of a ^{68}Ge-^{68}Ga generator.

^{68}Ge/^{68}Ga Generator

The ITG Medical Isotopes ^{68}Ge/^{68}Ga generator is used to produce a gallium chloride (^{68}Ga) solution for labeling of radiopharmaceuticals [8]. Table 2 shows the physical properties of the isotopes ^{68}Ge and ^{68}Ga.

Table 2: Physical Properties of Isotopes ^{68}Ge and ^{68}Ga [9].

Parent Isotope	Half Life	Decay Type	Daughter Isotope	Positron Range (mm)
^{68}Ge	271 days	Electronic Capture (100%)	^{68}Ga	--
^{68}Ga	68 minutes	Positron Emission (89%)	^{68}Zn (stable)	3.48 (on the water)

2.2. Methods

^{68}Ga isotope was obtained by generator elution. For this, the connectors at the inlet and outlet of the generator were connected. Next, the inlet connector was coupled to a syringe containing 4 ml of HCl, (0.05 mol/l) and the outlet connector was coupled to a vacuum-sealed collection vial.

The HCl was then injected into the generator with the use of the syringe. The HCl solution circulated through the interior of the generator, passing through a radioactive column containing ^{68}Ga. At the outlet of the generator, eluate containing ^{68}GaCl3 was collected in the vacuum-sealed flask. The eluate was later diluted (~5MBq/ml) and used to fill the phantom.

To acquire the PET images, the simulator was filled with ^{68}Ga solution and then positioned in the center of the field of view (FOV) of the small animal PET scanner, as shown in Fig. 2. The acquisition and reconstruction of the PET images were performed using the LabPET 1.12.1 software, provided by the equipment manufacturer. Table 3 show the parameters used in these steps.

Figure 2: Simulator filled and positioned in the center of the FOV.

Table 3: Parameters for image acquisitions and reconstructions

Step	Parameter	Value
Image Acquisitions	Acquisition time	1 hour
	Activity	22.8 MBq
	Bed Position	1 Position
Image Reconstructions	Transverse FOV	46mm
	Algorithm	MLEM-3D
	Number of interactions	20
	Resolution	Standard (0.50 x 0.50 x 0.50) mm3

After reconstruction, the images were treated and analyzed using the AMIDE® software [10]. Graphs containing the line profile of the PET signal strength along the fillable channels were generated for each of their groups. For each manually chosen line, passing through the center of the channels of the analyzed group, the software exports files, in .txt format, containing the intensity of the PET signal as a function of the position.

Subsequently, the .txt files containing the line profiles, obtained in the previous step, were treated using the PeakFit® software [11]. In this software, graphs of each line profile were generated. The software allows the adjustment of the experimental curve using the peak deconvolution method. From the adjusted curves, it was possible to obtain the half-height widths (FWHM) of the peaks of interest.

3. RESULTS AND DISCUSSION

Figure 3 shows a PET image obtained for the ^{68}Ga-filled simulator. A qualitative figure analysis allows us to visually distinguish the channels of the G1 and G2 groups. From the G3 onwards, the system does not have sufficient spatial resolution to distinguish individual channels.

Figure 3: ^{68}Ga-PET image of the hot rod simulator.

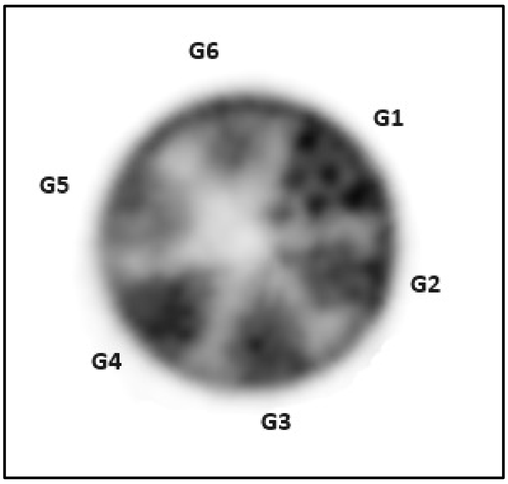
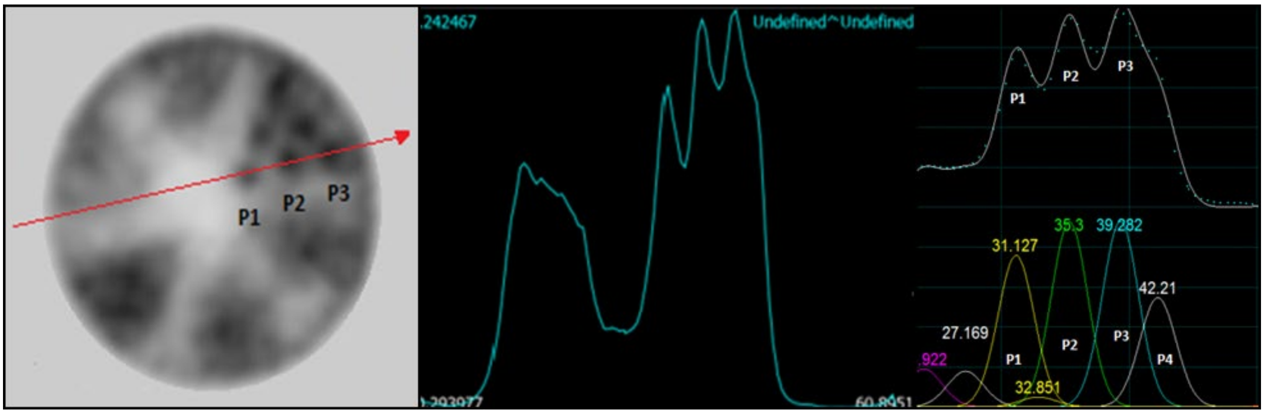


Figure 4 shows the results obtained in the stages of determination of the line profile and peak deconvolution for G1.

Figure 4: Obtaining and deconvoluting peaks of the line profile of group G1.



(A) (B) (C)

(A): Definition of the line, passing through the center of three fillable channels.
(B): Line profile determined for G1;
(C): Deconvolution of the peaks of the G1 line profile.
Upper: Curve adjusted with five Gaussians; Bottom: Gaussians used in the adjustment.

In Figure 4 C, the P4 peak refers to the simulant edge signal, while the P1, P2, and P3 peaks refer to the 2.0 mm fillable channels in G1.

Table 4 shows the results obtained after the analysis of the line profiles of Groups 1 and 2. As previously stated, the peaks referring to fillable channels cannot be resolved from the G3 group. In the table, it is possible to verify that the spatial resolution (FWHM) ranged from 3.15 mm to 4.39 mm, with mean values of (3.7 ± 0.6) mm for the G1 group and (3.6 ± 0.2) for the G2 group. These values are of the same magnitude as the positron range (3.48 mm).

In the simulator, the distances between the channels in groups G1 and G2 are 4.0 mm and 3.0 mm respectively. Based on the results in Table 4, the distances were calculated by the difference between the positions of the peaks. Table 5 shows the results obtained.

Table 4: Results of the Analysis of the Line Profiles of Groups 1 and 2

Group - Diameter (mm)	Peaks	Amplitude (U.A.)	Position (mm)	FWHM (mm)
G1 – 2.0	P1	0.19 ± 0.03	31.2 ± 0.4	3.63
	P2	0.21 ± 0.03	35.1 ± 0.1	3.15
	P3	0.23 ± 0.01	39.3 ± 0.2	4.39
G2 – 1.5	P1	0.16 ± 0.07	18.3 ± 1.3	3.77
	P2	0.16 ± 0.21	22.2 ± 2.8	3.68
	P3	0.14 ± 0.28	25.4 ± 2.3	3.44
	P4	0.13 ± 0.13	28.7 ± 2.2	3.33

Table 5: Results of Row Profiles from Groups 1 and 2

<table>
<tr><th colspan="7">Position of the peaks (mm)</th></tr>
<tr><th colspan="3">G1</th><th colspan="4">G2</th></tr>
<tr><th>P1</th><th>P2</th><th>P3</th><th>P1</th><th>P2</th><th>P3</th><th>P4</th></tr>
<tr><td>31.2 ± 0.4</td><td>35.1 ± 0.1</td><td>39.3 ± 0.2</td><td>18.3 ± 1.3</td><td>22.2 ± 2.8</td><td>25.4 ± 2.3</td><td>28.7 ± 2.2</td></tr>
<tr><th colspan="7">Distance Between Peaks (mm)</th></tr>
<tr><td>P1 a P2</td><td colspan="2">3.9</td><td>P1 a P2</td><td colspan="3">3.9</td></tr>
<tr><td>P2 a P3</td><td colspan="2">4.2</td><td>P2 a P3</td><td colspan="3">3.2</td></tr>
<tr><td rowspan="2">Average</td><td rowspan="2" colspan="2">4.1 ± 0.2</td><td>P3 a P4</td><td colspan="3">3.3</td></tr>
<tr><td>Average</td><td colspan="3">3.5 ± 0.4</td></tr>
</table>

The results in Table 5 indicate that the distance between the peaks obtained in the line profile adjustment is compatible with the actual distance in the simulator (G1: 4.0 mm; G2: 3.0 mm). This fact corroborates the methodology used in the analysis of the line profile.

The results indicate that spatial resolution of the system for ^{68}Ga isotope is approximately equal to the positron range (~3.5 mm). Previous studies by the LIM/SERAF/CDTN team using the ^{18}F isotope (0.62 mm positron range) and the

MicroPET Hot Rod Phantom obtained a spatial resolution of 1.2 mm [12]. This worsening in the spatial resolution of the system was already expected due to the greater penetration of the ^{68}Ga positron compared to the ^{18}F positron.

These quantitative results must be considered in preclinical PET image studies, especially in the analysis of small structures. Some organs like eye, thyroid, gall bladder, testicle, uterus, ovary, etc. may become difficult or even impossible to identify. In this sense, the experimental design must be very careful and preferably with additional morphological images from computed tomography or magnetic resonance imaging. It is important to consider the biodistribution of the ^{68}Ga-based radiopharmaceuticals and the implicit limitations caused in PET imaging due to the low spatial resolution associated with the use of the ^{68}Ga isotope.

4. CONCLUSIONS

This work allowed us to know the spatial resolution of the small animal's PET scanner of the LIM/SERAF/CDTN using the ^{68}Ga isotope. The value found (~3.5 mm) is approximately three times higher than the resolution of the system when using the isotope ^{18}F (~1.2 mm). The differences observed in spatial resolution values are due to the differences in positron ranges. The low spatial resolution associated to the ^{68}Ga isotope must be considered in the design of the experimental preclinical studies.

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REFERENCES

[1] CNEN. Comissão Nacional de Energia Nuclear. Instalações de Medicina Nuclar Autorizadas. Available at: https://appasp2019.cnen.gov.br//seguranca/cons-ent-prof/entidades-aut-cert.asp. Last accessed: 25 July 2023.

[2] CNEN. Comissão Nacional de Energia Nuclear. Relatório de Gestão CNEN 2022. Available at: https://www.gov.br/cnen/pt-br/acesso-a-informacao/transparencia-e-prestacaodecontas/arquivos_prestacaodecontas/relatoriodegestaocnen2022_publicado2.pdf/view. Last accessed: 25 July 2023.

[3] GONTIJO, R.M.G.; et al. Performance based on NEMA NU-4 2008 Standard of CDTN/CNEN's Small Animal PET Scanner**. Brazilian Journal of Radiation Sciences**, Belo Horizonte, v.10, n. 3, p. 1-17, 2022.

[4] SAHA, G.B. Biological Tests. **Basics of PET Imaging: Physics, Chemistry, and Regulations**. Ohio, US: Springer Publishing Co, 2015. 3th ed., p. 121, ISBN 978-1-4899-8471-5.

[5] CDTN. Centro de Desenvolvimento da Tecnologia Nuclear. Belo Horizonte, MG, Brazil. Available at: https://www.cdtn.br. Last accessed: 25 July 2023.

[6] GE HealthCare. Triumph Service Guide Technical Publication. Revision Draft 6, Copyright. Available at: http://www.gehealthcare.com. Last accessed: 25 July 2023.

[7] QRM-70121. QMR Micro-PET Hot-Rod Phantom. Available at: https://www.qrm.de/en/products/micropethotrodphantom#accordion_collapse_12024. Last accessed: 23 Jan. 2024.

[8] ITG Medical Isotopes. Available at: https://www.gruporph.com.br/en/generators/. Last accessed: 25 July 2023.

[9] DISSELHORST, J.A., et al. **Image-Quality Assessment for Several Positron Emitters Using the NEMA NU 4-2008 Stardars in the Siemens Inveon Small-Animal PET Scanner. The Journal of Nuclear Medicine**, US, v. 51, No.4. p. 610-617, 2010.

[10] AMIDE. Medical Image Data Analysis. v.0.9.0. Available at: https://amide.sourceforge.net. Last accessed: 23 Jan. 2024.

[11] PEAKFIT. Peak Separation and Analysis Software. Available at: https://grafiti.com/product/peakfit-free-trial/. Last accessed: 23 Jan. 2024

[12] SOUZA, G.A.C. et al. Spatial resolution of a preclinical PET tomograph**. Brazilian Journal of Radiation Sciences**, v. 9, n. 01A, p. 1-18, 2021.

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