Abstract—This article presents the performance assessment study of the PET component of the IRIS PET/CT according to the National Electrical Manufacturers Association (NEMA) NU 4–2008 standard.

The IRIS PET/CT is a high-resolution integrated system for PET and CT imaging of small animals. We evaluated the performance of the PET system, carrying out the following measures: spatial resolution, sensitivity, counting rate capabilities, and image quality parameters. Furthermore, two examples of in vivo experiments are shown. The average energy resolution for a whole module is 14% at 511 keV. The maximum absolute sensitivity for a point source at the center of the field of view is 8.0±1.1% for 250-750 keV energy window and 6.6±1.0% for 350-750 keV. The scatter fraction for mouse-like and rat-like phantoms are 15.6% (250-750 keV) and 22.4% (350-750 keV), respectively. Recovery coefficients were measured with the image-quality phantom, providing good results with an image uniformity of 7%. The imaging performance of the IRIS PET are confirmed in the animal experiments. With the IRIS PET/CT it was possible to derive the time activity curve for various regions of interest with time frame duration down to 5 s, thus enabling the possibility to derive the tracer input function.

Index Terms— IRIS PET/CT, Pre-clinical PET scanner, Molecular imaging, Performance evaluation.

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I. INTRODUCTION

The IRIS PET/CT features state of the art technology and it is commercially available† as a solution for pre-clinical studies on mice and rats. The scanner comprises a full ring PET and a high resolution CT system placed sequentially like in clinical PET/CT scanners [1]. This article presents the performance assessment study of the PET component of the system following the National Electrical Manufacturers Association (NEMA) NU 4–2008 standard [2].

In this paper, the NEMA recommended measurements for evaluating the performance of the PET component itself, i.e., spatial resolution, scatter fraction, count losses, random coincidence rate, sensitivity and image quality are reported. In addition, an example of a typical pixel map and a typical energy spectrum are shown as well as two examples of in-vivo measurement on mice.

The results presented in this paper refer to the performance of the IRIS PET/CT now installed at the Laboratory of Imaging Biomarkers of the CNR Institute of Clinical Physiology (Pisa, Italy), where all the reported measurements were performed.
This scanner. It features 16 Data Acquisition (DAQ) boards signal passes through a constant fraction discriminator (CFD) conditioned by fast pre-amplifiers. The amplified last dynode locations. Both position and last dynode signals are standard “Anger logic” is used for reconstructing event simplicity and good performance [4]. The SCD reduces the 8 signals of each PMT into 8 x + 8 y signals. These signals enter a passive resistive chain that further reduces the number of signals to four (X_A, X_B, Y_A, Y_B). A standard “Anger logic” is used for reconstructing event locations. Both position and last dynode signals are conditioned by fast pre-amplifiers. The amplified last dynode signal passes through a constant fraction discriminator (CFD) to produce the timing signal.

The position signals generated by the front-end are sent to a back-end data acquisition system, specifically designed for this scanner. It features 16 Data Acquisition (DAQ) boards based on peak-sensing 12-bit A/D converters, which are hosted on a FPGA-based mainboard. The mainboard hosts a Control FPGA, powers the whole system and provides data connection to PC via USB 2.0 [5]. The main processing tasks carried out by the Control FPGA are the data transfer management, the event tracking, the run-time configuration and status control. The mainboard FPGA is a high-end model (Stratix III, Altera Corp., San Jose, CA) which provides high memory resources, that are needed for data buffering, high number of I/O pins and low propagation delays, the latter required for prompt coincidence monitoring.

Digital timing signals are fed to the Control FPGA for coincidence processing [6]. Events from two modules are accepted when their arrival time is within a maximum difference of 2.6 ns, corresponding to an actual coincidence window (2τ) of 5.2 ns. When a coincidence is detected in an allowed module pairs the corresponding DAQs are triggered to perform signal digitization. In this way, only coincidences are acquired. The random events are acquired using a random single event acquisition [7]. Following this implementation, the delayed coincidence system generates a delayed timing signal on all modules. When a delayed coincidence is detected, only the event position signals on the non-delayed side are acquired. This helps minimize acquisition dead time by avoiding the complication of acquiring the signals produced in the delayed side. Random LOR are then generated by combining two random singles. The coincidence processor rejects multiple coincidences.

Events are sent to the local data acquisition PC in the form of data packets and are stored in a list-mode format. In order to optimize the data bandwidth, the size of the packets is varied dynamically according to the input data rate. As the input rate increases the data packed becomes larger thus keeping the rate of packet transmission approximately constant in time. On average, each data packet is sent every 0.5 s. The list-mode format contains the four position signals, the module identifier, and other event tags (e.g., gating signals or random coincidence flag). Each data packet includes the information on the coarse time stamp, together with the single, the coincidence and the random count rates.

Images can be reconstructed with a multi-core line of response (LOR) based 3D Maximum Likelihood Estimation Maximization (MLEM) or Ordered Subset Estimation Maximization (OSEM). The statistical models used for the reconstruction are evaluated with the Siddon multi-ray based algorithm described in [8]. A variance reduction technique is implemented in the post-processing phase to reduce the statistical fluctuation on the random data [7]. A Defrise-like normalization [9] and a standard random correction are also implemented. Events can be corrected for dead-time and decay-time and attenuation correction is implemented with a CT-based μ-maps.

The IRIS PET/CT can be fully controlled by the user with a web-based Graphical User Interface (GUI). The GUI allows the user to create animal studies and multimodality acquisition workflows, including the possibility of customizing both the post-processing and the image reconstruction protocols.

### II. MATERIALS AND METHODS

#### A. Scanner Description

The PET component of the scanner consists of 16 modules arranged in two octagonal rings (figure 1). Each module can acquire coincidences with the six opposing modules, three belonging to the same ring and three belonging to the other. The IRIS/PET field-of-view has 95 mm axial coverage and a transaxial coverage of 80 mm. Each module comprises a matrix of 27 (transaxially oriented) x 26 (axially oriented) (702 in total) lutetium-yttrium orthosilicate crystals doped with cerium (LYSO:Ce) of 1.6 mm x 1.6 mm x 12 mm with a pitch of about 1.7 mm. The matrix is directly coupled to a 64 anodes PMT (H8500C, Hamamatsu Photonics K.K., Hamamatsu, Japan). Each module is completely independent and PMT. This module arrangement creates an axial gap approximately 6.8 mm wide between the two rings (four times the pixel pitch). A summary of PET system specification is reported in table I.

The same modularity is implemented at the level of the acquisition electronics. The output signals from each PMT pass through a front-end conditioning stack made of a coding board, a pulse shape preamplifier and a timing board.

The coding board consists of a Symmetric Charge Division (SCD) [3] resistive network, which is implemented for its simplicity and good performance [4]. The SCD reduces the 8 x 8 signals of each PMT into 8 x + 8 y signals.

These signals enter a passive resistive chain that further reduces the number of signals to four (X_A, X_B, Y_A, Y_B). A standard “Anger logic” is used for reconstructing event locations. Both position and last dynode signals are conditioned by fast pre-amplifiers. The amplified last dynode signal passes through a constant fraction discriminator (CFD) to produce the timing signal.

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The IRIS PET/CT can be fully controlled by the user with a web-based Graphical User Interface (GUI). The GUI allows the user to create animal studies and multimodality acquisition workflows, including the possibility of customizing both the post-processing and the image reconstruction protocols.

### TABLE I

<table>
<thead>
<tr>
<th>Module</th>
<th>LYSO:Ce</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal material</td>
<td></td>
</tr>
<tr>
<td>Crystal pixel size (mm³)</td>
<td>1.6 x 1.6 x 12</td>
</tr>
<tr>
<td>Crystal pixel pitch</td>
<td>1.69 mm</td>
</tr>
<tr>
<td>No. of crystals</td>
<td>702 (27 x 26)</td>
</tr>
<tr>
<td>System</td>
<td></td>
</tr>
<tr>
<td>No. of modules</td>
<td>16 (8 x 2)</td>
</tr>
<tr>
<td>No. of crystals</td>
<td>11232</td>
</tr>
<tr>
<td>Inner diameter</td>
<td>110.8 mm</td>
</tr>
<tr>
<td>Gantry aperture</td>
<td>100 mm</td>
</tr>
<tr>
<td>Axial FOV</td>
<td>95 mm</td>
</tr>
<tr>
<td>Transaxial FOV</td>
<td>80 mm</td>
</tr>
<tr>
<td>Dataset</td>
<td></td>
</tr>
<tr>
<td>No. of lines of response</td>
<td>23654592</td>
</tr>
<tr>
<td>Coincidence scheme</td>
<td>1 vs 6</td>
</tr>
<tr>
<td>No. module pairs</td>
<td>48</td>
</tr>
<tr>
<td>Coincidence window (ns)</td>
<td>5.2 (2τ)</td>
</tr>
</tbody>
</table>
parameters. The same GUI is used for hardware control and monitoring.

The PET component of the IRIS PET/CT is directly attached to the back of the high precision CT gantry and can spin around the object. This enables the unique possibility to perform rotational acquisitions where coincidence data are acquired at different angular positions in "step-and-shoot" mode. Although the detector rotation in the IRIS PET/CT is not strictly necessary due to the almost full angular coverage of the detector system, such a modality can have advantages in terms of image quality due to the more uniform line-of-response sampling of the field of view. This makes this acquisition mode particularly well suited for those cases where image quality is critical. The performance evaluation reported in this paper is made with non-rotating acquisition scans only, as this modality is the one more commonly used in routine protocols.

B. Flood map, energy resolution and normalization

A planar phantom with a hollow region of 110 mm × 95 mm × 2 mm is used for both creating the calibration flood histograms and performing the detector normalization. The phantom was filled with 7 MBq of $^{18}$F solution and placed in the Field-Of-View (FOV) with the longest size along the scanner axis in four different angular position: 0° (vertical), 45°, 90° and 135°. Data acquisition was performed for 30 minutes per position.

The calibration of each module consists of four steps: flood map generation, pixel centers identification, generation of crystal look-up table and energy calibration. First, the flood maps are generated for each module using the data acquired at the four angular positions. The flood map is a 2D histogram of the reconstructed event locations (see figure 2, left) where the peaks correspond to crystal centers. A semi-automatic calibration software identifies the peaks (blue dots in figure 2, right) and creates pixel identification look-up tables (regions in gray in figure 2, right). Using this look-up table, the energy spectrum of each crystal pixel is generated and calibrated in keV using the full energy peak as the reference for the 511 keV value. The energy spectrum of a module is obtained by summing up all the calibrated spectra of its pixels. The energy resolution of the PET system (reported in percent) was evaluated as the average value of the full width at half maximum of the full energy peak of each module divided by 511 keV.

The same acquisition is used to perform the LOR-based stepwise normalization: for each phantom position, those coincidences involving at least one of the modules lying close to the phantom edges were discarded (see figure 3). For example, when the planar phantom is positioned at 0° (figure 3, left), all the coincidences involving the modules painted in white (1 and 5) are discarded, while all the coincidences among the modules painted in gray are used for normalization. The same rule is applied when the phantom is positioned at 45° (figure 3, right), 90° and 135°. Hence, for each position, 28 of 48 detector pairs are used for collecting normalization data when considering both detector rings. With this procedure, all the pairs are acquired at least twice (opposing pairs three times) to maximize counting statistics, and reducing statistic fluctuations.

C. Spatial resolution

According to the NEMA standard a $^{22}$Na point source (sphere) with an active dimension of 0.25 mm diameter and centered in 1 cm$^3$ cast acrylic cube (Eckert & Ziegler Isotope Products, Valencia, CA, model MMS09) was used to perform spatial resolution assessment. At the time of the measurement its activity was 1.55 MBq.

The source was placed in the axial center of the FOV, and at one-fourth of the axial FOV from the center of the axial FOV, at the following radial distances from center: 5 mm, 10 mm, 15 mm, 25 mm. Data were acquired for 120 s. Though the NEMA NU-4 standard indicates filtered back projection (FBP) as reconstruction algorithm for the spatial resolution measurements, this algorithm is not provided by the manufacturer. Results obtained with the MLEM algorithm are reported instead, performing 50 iterations.

However, the non-negativity constraints of this method applied to reconstruct a point source with no background and the non-linearity of MLEM artificially enhance the resolution [10]. Therefore, the FWHM of the reconstructed point source cannot be used to predict the ability of the system to resolve two adjacent hot spots. For this reason, we have performed an additional experiment applying an artificially generated warm background to the point source data, following the method described in [10] and performing 500 MLEM iterations. Using

Fig. 2. Flood map of one module (left) and relative crystal look-up table (right). Blue dots are the centers of the pixels as identified by the semi-automatic algorithm.

Fig. 3. Picture illustrating the stepwise normalization procedure for one ring of the detector: all the coincidences involving the modules in white are discarded, whereas the others are used for normalization. For example, the picture portrays two normalization phantom positions: source at 0° (left) and source at 45° (right).
this method, two representative positions only were studied: 5 mm radial distance at the axial center of the FOV and 25 mm radial distance at one-fourth of the axial FOV. In each of the two images, the point source contrast (C), defined as: \( C = \frac{reconstructed \ point \ peak \ intensity \ - \ background \ intensity - 1}{background \ intensity} \), was measured. In this case, point source response functions were obtained by subtracting the reconstructed background image from the point source + background images.

In all cases described above, the voxel size was set to the minimum available size, i.e., 0.420 mm \( \times 0.420 \ mm \times 0.855 \ mm \). An energy window of 250–750 keV was applied to the reconstructed data. The FWHM and FWTM of the point source response function along the radial, tangential and axial directions were determined following the NEMA suggested procedure. Results were not corrected for positron range effect or source size.

D. Scatter Fraction, Counting Rate Losses, and Random Coincidence Rate Measurements

The purpose of these measurements was to evaluate the scanner performance in terms of the counting rate capability, the fraction of acquired events undergoing scatter (scatter fraction) and the rate of events originating from uncorrelated photons pairs (random coincidences).

Due to the size of the available field of view, two phantoms sizes were used for this characterisation: the mouse-like and the rat-like. According to the protocol the mouse-like phantom is made of a solid high-density polyethylene cylinder (density 0.96 g/cm\(^3\)) 70 mm long and 25 mm in diameter, with a cylindrical hole (3.2 mm diameter) drilled parallel to the central axis, at a radial distance of 10 mm. The rat-like phantom has a similar geometry but it is 150 mm long and it has a diameter of 50 mm. The cylindrical hole (3.2mm diameter) is at a radial distance of 17.5 mm.

Two different acquisitions were performed using the two phantoms. For the mouse-like phantom the central 60 mm were filled with 20 MBq of \(^{18}F\)-FDG mixed in water. The same amount of activity was used for the rat-like phantom but, in this case, the activity encompassed the central 140 mm of the phantom. In order to reduce the output data file size, an acquisition duty cycle of 10% was applied, i.e., a protocol with relatively short acquisitions followed by a waiting time of nine times its duration was applied. During the activity decay, the duration of each acquisition (and thus the waiting time) was progressively increased to still acquire enough counts in accordance to the NEMA protocol. In both cases the acquisition lasted for 14 hours.

Data were processed with no correction for dead-time, decay, attenuation or random counts. Measured random counts (reported as random event rate or \( R_r \)) were estimated with a delayed coincidence window method and stored separately from the coincidence counts (total event rate or \( R_{TOT} \)).

An energy window of 250-750 keV was used to process data from the mouse-like phantom, while in the case of the rat-like phantom the low energy threshold was set to 350 keV. To evaluate the intrinsic true event rate (\( R_{int} \)) due to the radiation of the \(^{18}F\)-FDG present in the LYSO crystals, a separate acquisition with no activity in the FOV was performed. The appropriate energy window was then applied to evaluate \( R_{int} \) for the two cases.

The final acquisition of the sequence, where count loss rates and random event rates were below 1.0% of the true event rate (\( R_t \)), was used to determine the scatter fraction (\( SF \)). For this purpose only, data from the final acquisition were sorted into 2D sinograms. Oblique sinograms were collapsed into a single sinogram by single-slice rebinning (SSRB) with a 0.855 mm slice thickness. The method suggested by the NU 4 - 2008 protocol was applied to the 2D sinograms to calculate the scatter fraction for both phantoms.

The NU 4 - 2008 document suggests to use the same procedure for the calculation of the scatter fraction to yield, for each acquisition, number of random plus scattered event’s count rates (\( R_{r+s} \)). The system true event rate \( R_t \) could then computed as:

\[
R_t = R_{TOT} - R_{r+s},
\]

where \( R_{TOT} \) can be written as:

\[
R_{TOT} = R_t + R_s + R_s + R_{int}
\]

However, for systems that directly estimate random coincidences, this is an unnecessary complication of the procedure. In fact, the random event rate can be independently calculated, and under the assumption that the scatter fraction does not vary with the activity level, the scatter count rate is always the same fraction (\( SF \)) of the prompts count rate (\( R_t + R_s \)), i.e., equation 3 is valid for any count rate.

\[
R_s = SF \times (R_t + R_s)
\]

Hence, instead of using equation 1 to estimate \( R_s \), the true event rate can be calculated combining equations 2 and 3, as:

\[
R_t = (R_{TOT} - R_s) \times (1 - SF)
\]

This latter method is the one used in this work.

The noise equivalent count rate \( R_{NEC} \) is then calculated using the formula:

\[
R_{NEC} = R_t^2 / (R_{TOT} + R_t)
\]
total sensitivity obtained averaging sensitivity results for the whole FOV ($S_{FOV}$) is taken as representative of $S_R$.

$F$. Image quality study

The NU4-2008 standard prescribes the use of a specific image quality phantom. The suggested phantom mimics a total body imaging study of a mouse-sized animal with a uniform hot region, as well as hot lesions and some cold areas. The uniform region of the phantom is composed of a fillable cylindrical chamber with 30 mm diameter and 30 mm length, and a solid part with five fillable rods with diameters of 1, 2, 3, 4 and 5 mm in direct contact with the uniform region, in order to have the same activity concentration in all hot regions.

The phantom was filled with 3.7MBq (measured in a Capintec CRC-15r dose calibrator) of $^{18}$F-FDG mixed in water and placed in the central part of the FOV. The duration of the scan was 20 minutes.

Images were reconstructed using OSEM with 6 subsets, with an image matrix size of 201×201×120 and a voxel size of 0.420 mm × 0.420 mm × 0.855 mm, performing 8 iterations. The energy window was set to 250-750 keV.

Using the reconstructed images of this phantom, both the image noise properties and the spatial resolution were analyzed. A CT based attenuation correction was implemented. The CTAC map was generated from a CT scan taken with the following settings: 80 kV, 1 mA, 576 angles over 360°, 20 s total scan time. For the current experiment, the absorbed dose for the CTAC scan was 30 mGy. Further experiments are ongoing to assess the possibility of dose reduction for CTAC purposes.

The NU 4 - 2008 protocol indicates the image roughness defined as in [11] as a measure of the uniformity of the image. Image roughness, is usually intended to quantify the spatial noise perceived in an individual image by evaluating the coefficient of variation of the pixel values belonging to a certain region of the image. According to the protocol the central uniform region of the image quality phantom was analyzed and the image roughness ($%IR_{UR}$) was evaluated as follows:

$$\%IR_{UR} = 100 \frac{STD_{UR}}{A_{UR}}$$

where $STD_{UR}$ is the standard deviation measured in a volume of interest (VOI) of 22.5 mm diameter by 10 mm long selected within the uniform region of the phantom and $A_{UR}$ is the mean activity value in the same VOI.

The recovery coefficients ($RC$) relative to the five rods are calculated as:

$$RC_d = \frac{max_{j \in ROI_d} (T_j)}{A_{UR}}$$

where $d$ is the rod diameter, $T_j$ is the activity value relative to the voxel $j$ in the single slice image obtained by averaging the slices belonging to the central 10 mm length of the rods, $ROI_d$ is the circular region of interest (ROI) of diameter $2d$ selected around the rod of diameter $d$ in the averaged image.

The standard deviation of the recovery coefficients ($%STD_{RC}$) was calculated as:

$$%STD_{RC} = 100 \sqrt{\frac{STD_{profile}^2}{\bar{T}_{profile}^2} + \frac{STD_{UR}^2}{T_{UR}^2}}$$

where $STD_{profile}$ is the standard deviation of values measured along the rods in the axial direction (taken at the same location of $max_{j \in ROI_d}$) and $\bar{T}_{profile}$ is the average activity value calculated along the same lines.

$G$. Animal study

All images presented in this Section have been obtained during animal experiments that were conducted in accordance with the Italian Law D.L. 26/2014, implementation of the 2010/63/EU directive for animal protection in scientific experiments. All animals were handled by qualified veterinary personnel following internal standards of IFC-CNIR, after approval of the experimental protocol by the Italian Ministry of Health.

One example of an animal study is reported to show the imaging capability of the PET component of the IRIS PET/CT. A CD1 mouse weighting 51 g was injected with 7.45 MBq of $^{18}$F-FDG. The animal was injected by hand via a tail vein, with a typical injection duration of about 2-3 s (bolus injection). A dynamic PET scan immediately started for a total duration of 60 min. The duration of time frames was chosen in order to follow the fast tracer dynamic in the first seconds. In particular, the following time frame sequence was selected: 8 (frames) × 5 s + 8 × 10 s + 3 × 40 s + 2 × 60 s + 2 × 120 s + 10 × 300 s. Prior to the injection the mouse underwent a fast medium-dose CT scan (80 kV, 1 mA, 20 s total scan time). The CT reconstruction was performed with standard ramp filter and with a voxel size of 0.16 mm. In PET, images were reconstructed for the various time frames of the scan with OSEM, 6 subsets, 8 iterations. An image size of 101×101×120 with a cubic voxel size of 0.855 mm × 0.855 mm × 0.855 mm was used for this reconstruction, being this voxel size the standard one for dynamic scans. Each time frame was reconstructed independently. Data from the time interval 900 s
were obtained by scaling the reconstructed activity (in a.u.) by a calibration factor obtained by reconstructing, with the same protocol, a uniform cylinder of well-known activity concentration. An additional 5 min PET scan was performed after 95 min from injection. In this case, MLEM with 60 iterations, on a matrix size of 201×201×120 (0.420 mm × 0.420 mm × 0.855 mm voxel size) was used for image reconstruction. All images were reconstructed using the 250-750 keV energy window.

III. RESULTS

A. Pixel identification and energy resolution

All crystal elements were fully identified (figure 2) and the average measured energy resolution for a whole module is 14% at 511 keV. This value was obtained after energy calibration of each crystal, summing up all the spectra of the whole matrix. Figure 4 shows a typical energy spectrum of a single module.

B. Spatial resolution

Radial, tangential and axial resolutions (FWHM and FWTM) for each location (5 mm, 10 mm, 15 mm and 25 mm), as well as the image pixel size and slice thickness, are reported for both axial positions in Table II.

For the point source measurement with a warm background, the background level was increased until the point source contrast ($C$) was below 0.1 as suggested by [10]. For the position at axial center of the FOV and 5 mm radial offset the measured radial, tangential and axial FWHM were 1.78 mm, 1.66 mm and 1.68 mm, respectively, with a measured contrast $C = 0.09$. For the position at quarter axial FOV and 25 mm axial offset the measured radial, tangential and axial FWHM were 2.30 mm, 1.86 mm and 1.46 mm, respectively, with a measured contrast $C = 0.09$.

C. Sensitivity

The maximum absolute sensitivity for a point source at the center of the field of view ($S_{FVoV}$) is 8.0% for 250-750 keV energy window and 6.6% for 350-750 keV. These values are not corrected for the attenuation from the acrylic cube surrounding the point source.

These values are among the highest in the market [12-15]. These measures are both affected by an error due to the accuracy of ±15% of the real activity of the used $^{22}$Na by the manufacturer (Eckert & Ziegler) for non-traceable sources.

The absolute system sensitivity for the mouse ($S_m$) and rat ($S_r$) representative lengths are 5.0% and 4.0%, respectively, the latter being also representative of $S_{FVoV}$. Both values are evaluated using the 250-750 keV energy window.

D. Scatter Fraction, Counting Rate Losses, and Random Coincidence Rate Measurements

Figure 5 reports the plot of $R_{TOT}$, $R_n$, $R_s$, and $R_{NEC}$ for mouse-like and rat-like phantoms, respectively. The peak of the NEC curve for the mouse-like phantom is 185 kcps reached at an activity of 14 MBq, while the peak of the curve for the rat-like is 40 kcps at 10 MBq. The measured scatter fraction for mouse-like and rat-like phantoms are 15.6% (250-750 keV energy window) and 22.4% (350-750 keV energy window), respectively.

### Table II

<table>
<thead>
<tr>
<th>POINT SOURCE MEASUREMENT RESULTS OBTAINED WITH 3D MLEM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At axial center</strong></td>
</tr>
<tr>
<td>Image pixel size (mm): 0.420 mm x 0.420 mm - Slice thickness: 0.855 mm</td>
</tr>
<tr>
<td>5 mm</td>
</tr>
<tr>
<td>FWHM</td>
</tr>
<tr>
<td>R</td>
</tr>
<tr>
<td>T</td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td><strong>At quarter axial FOV from center</strong></td>
</tr>
<tr>
<td>Image pixel size (mm): 0.420 mm x 0.420 mm - Slice thickness: 0.855 mm</td>
</tr>
<tr>
<td>5 mm</td>
</tr>
<tr>
<td>FWHM</td>
</tr>
<tr>
<td>R</td>
</tr>
<tr>
<td>T</td>
</tr>
<tr>
<td>A</td>
</tr>
</tbody>
</table>

Values are reported in mm.
E. Image quality study

Figure 6 shows some more representative slices (coronal and sagittal) of the IQ phantom image obtained with OSEM (6 subsets, 8 iterations) which is the standard setting for animal study in our laboratory. In this image, the mean uniformity value in the uniform region is about 7%.

Table III reports a summary of the measurement of the values of the recovery coefficients for the five rods. The spill-over ratio (SOR) was measured for both water-filled and air-filled cold regions of the IQ phantom. Results are reported in table IV.

F. Animal study

Twelve consecutive horizontal slices of the image obtained from the acquisition interval 900-1800 s of the dynamic scan are shown in figure 7. Small structures such as harderian glands, kidneys and heart walls and cavities are well visible.

The time activity curve (TAC) for the left ventricle (LV), myocardium, brain, left and right kidneys and bladder is shown in figure 8. The TAC plot has been restricted to the first 1350 s from injection to emphasize the more time-varying behaviour of the tracer concentration in the relevant organs.

In figure 9, the fused PET/CT image is shown. PET data are relative to the 95-100 min time interval. In this case, the long post-injection delay before PET scan (95 min) was chosen to have the best compromise between tracer washout from the blood pool and myocardial uptake of \(^{18}\)F-FDG so as to ensure the best visualization of the myocardial walls. The small voxel size \((0.420 \times 0.420 \times 0.855 \text{ mm}^3)\) and as well the MLEM reconstruction with 60 iterations were used to provide the highest possible spatial resolution.

No gating for cardiac and respiratory motion was applied for this case. In figure 9, bottom, the same PET image was reoriented following the standard short-axis and long-axis representation recommended by the American Heart Association (AHA) for cardiac imaging studies. The tracer distribution in the myocardial walls of both left and right ventricles is visible with the chosen scanning and reconstruction setup, even though partial volume effects must be taken into account for quantification of both activity concentrations in walls and cavities.
IV. DISCUSSION

The PET component of the IRIS PET/CT system was evaluated in its performance from pixel identification and energy resolution to performance assessment study that was based on the NEMA NU 4 - 2008 protocol.

Because of the good separation between pixels (as shown in Figure 2), the identification procedure provides very stable results and requires minimal user interaction. Consequently, also the energy calibration procedure becomes easier. The obtained energy resolution of 14% is excellent in comparison to other available systems [12-15].

The NEMA NU 4 – 2008 was applied and only some minor modifications were necessary to adjust the procedure to our specific system. In particular, the spatial resolution was measured with ML EM because FBP was not provided by the manufacturer.

The spatial resolution evaluated in this way shows a uniform behaviour with minimal radial elongation in the central 5 cm of the field of view and results are coherent with the scintillator matrix pitch of 1.7 mm.

A further adjustment of the protocol refers to the way the random plus scatter event count rate ($R_{r+s}$) is calculated, as detailed in section “Material and Methods - Scatter Fraction, Counting Rate Losses, and Random Coincidence Rate Measurements”. This approach was used in other works as well, e.g., [12].

The measured absolute sensitivity is among the highest of commercially produced small animal PET/CT systems. This allows the IRIS PET/CT system to produce good quality images even when using low activity levels, close to or below 1 MBq. It must also be noted that according to the NEMA NU4-2008 protocols the sensitivity values are not corrected for the attenuation from the source container. Other works, such as [12], considered a 12% sensitivity loss as the effect of the attenuation from the acrylic cube surrounding the source. Considering this effect, the source maximum sensitivity values at CFOV can be rescaled to 9.0% and 7.4% for the two considered energy windows, respectively.

The image quality study using the NEMA suggested phantom has indicated noise levels and recovery coefficients that are adequate for mouse and rat studies and are similar to those presented for systems with a similar pixel pitch [13]. The spill-over ratio values measured in the water-filled (0.11) and air-filled (0.11) cold regions confirmed the accuracy of the CT-based attenuation correction procedure.

IRIS PET/CT count rate performance is lower than that of other similar systems such as [12], showing a peak NEC for mouse and rat sized phantoms in the 10-14 MBq range. However, this is not an issue in the routine experiments in our laboratory and others [12], where typical injected activities are in the 1 to 10 MBq range.

Fig. 8. Time activity curve for the left ventricle (LV), myocardium, brain and left and right kidneys and bladder obtained from the mouse dynamic scan. Each point of the plot corresponds to a single time frame image.

Fig. 9. Top, example of a PET/CT image of a 51 g CD1 mouse injected with 7.45 MBq of $^{18}$F-FDG. The CT scan was performed at 80 kV, 1 mA, 20 s total scan time, and CT image was reconstructed with a cubic voxel size of 0.16 mm (display min-max: [-300 HU; 1000 HU]). The PET scan was performed in the interval 95-100 min after injection, 250-750 keV energy window, reconstructed with MLEM, 60 iterations, with a voxel size of 0.420 mm $\times$ 0.420 mm $\times$ 0.855 mm. Bottom, multi-planar reformation of a cardiac region of interest of the PET image shown above. Images are shown in standard short-axis (top left), vertical long axis (top-right) and horizontal long axis (bottom-left). Even without gating for cardiac and respiratory motion, both left ventricle and right ventricle cavities and walls are clearly visible.
The imaging performance of the IRIS PET are confirmed in the animal experiment. For the high scanner sensitivity, it was possible to derive the time activity curve for various regions of interest with time frame duration down to 5 s, thus enabling the possibility to derive the tracer input function.

The good capabilities of the IRIS PET in terms of spatial resolution are evident from the cardiac images in figure 9, where even without the application of gating techniques for cardiac and respiratory motion, both the left and right ventricle cavities and walls are clearly displayed. Of course, quantitative corrections for partial volume and spill-over effects must be applied for reliable quantification from these images.

Due to the lack of the FBP reconstruction algorithm, it was not possible to derive the system spatial resolution in compliance with the NEMA NU-4 protocol. Although not representative of the true system resolvability, the results obtained with the point source measurement (reported in table II) can be used to estimate the spatial variability of the point source spread function at different contrasts.

The FWHM measurements obtained with a warm background may be larger than those obtainable with a higher contrast source. Hence, these results provide an upper bound for the true system spatial resolution and can be used to compare the IRIS PET to other PET systems.

V. CONCLUSION

We have evaluated the performance of the PET component of the IRIS PET/CT system following the NEMA NU 4 – 2008 standard. The IRIS PET/CT compares very well to other small animal PET systems. The high sensitivity is reflected by the possibility to generate time activity curves with short time frames. The spatial resolution, image quality and count rate capability are adequate for mice and rat imaging in the pre-clinical routine at our laboratory.

REFERENCES


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