Evaluation of the performance of the YAP-(S)PET scanner and its application in neuroscience

Nicola Belcari\textsuperscript{a,}\textsuperscript{*}, Alberto Del Guerra\textsuperscript{a}, Antonietta Bartoli\textsuperscript{a}, Daniele Bianchi\textsuperscript{b}, Marco Lazzarotti\textsuperscript{b}, Luca Sensi\textsuperscript{b}, Luca Menichetti\textsuperscript{c}, Michela Lecchi\textsuperscript{d}, Paola A. Erba\textsuperscript{e}, Giuliano Mariani\textsuperscript{e}, Giovanni U. Corsini\textsuperscript{f}, Paola Sgad\textsuperscript{f}a

\textsuperscript{a}Department of Physics “E. Fermi” and Center of Excellence “AmbiSEN”, University of Pisa, and INFN, Sezione di Pisa, Pisa I-56127, Italy
\textsuperscript{b}I.S.E. s.r.l. Vecchiano, Pisa, Italy
\textsuperscript{c}IFC-CNR, Pisa, Italy
\textsuperscript{d}University of Milan, Milan, Italy
\textsuperscript{e}Nuclear Medicine Section, University of Pisa, Pisa, Italy
\textsuperscript{f}Department of Neuroscience, University of Pisa, Pisa, Italy

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Abstract

This paper presents the performance evaluation of the small animal scanner YAP-(S)PET, both in PET and SPECT modalities following preliminary NEMA standards for small animal PET. Data are taken with a new version of the scanner that is installed at the IFC-CNR in Pisa (Italy) within the framework of the Center of Excellence AmbiSEN of the University of Pisa. This paper also reports some preliminary SPECT applications in neuroscience using $^{123}$I-FP-CIT (DaTSCAN).

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1. Introduction

The YAP-(S)PET \cite{1,2} is the only small animal scanner that combines the PET and SPECT techniques on a single gantry. It is made up of four detector heads: each one is composed of a $4\text{ cm} \times 4\text{ cm}$ YAP:Ce matrix of $20 \times 20$ elements, $2 \times 2 \times 25 \text{ mm}^3$ each, coupled to a PS-PMT. Due to the relatively large solid angle subtended by each crystal matrix the system is subject to an appreciable pile-up probability. In order to improve the count rate capabilities, a completely new and faster readout electronics has been recently installed. The new electronics offers a reduced system dead time leading to a maximum acquisition rate ten times higher than the previous one. The new circuitry also includes a proprietary pile-up rejecting technique.

We have characterized the performance of the YAP-(S)PET scanner in both PET and SPECT modalities in terms of absolute sensitivity, spatial resolution and image quality (Derenzo phantom and NEMA \cite{3} phantom). PET scatter fraction and count rate performance (NEC) have been also evaluated using a mouse-sized phantom.

2. Performance evaluation

2.1. Spatial resolution

In PET mode, the spatial resolution was measured using a $^{22}$Na point source (1 mm \textit{Ø}) positioned at the center of the field-of-view (CFOV) and moved radially with 0, 3, 8 and 13 mm offset. For each position, the radial (R), transaxial (T) and axial (A) FWHM are measured. The spatial resolution at CFOV, using the wide open energy

\textsuperscript{*}Corresponding author. Tel.: +39 050 2214941; fax: +39 050 2214333. E-mail address: belcari@df.unipi.it (N. Belcari).
window (50–450 keV) is about 2.4 mm \( \times \) 2.4 mm \( \times \) 2.0 mm using FBP and 1.9 mm \( \times \) 1.9 mm \( \times \) 1.9 mm \( (R \times T \times A) \) using EM [4] with 10 iterations. Using the high spatial resolution energy window the spatial resolution is about 5–10% better. The volume resolution using EM is well below 10 mm\(^3\) over the whole FOV (Fig. 1).

In SPECT mode a glass capillary filled with \(^{99m}\)Tc solution was used for the evaluation of spatial resolution in the transaxial plane. The FWHM of the reconstructed image profile, constant over the whole FOV, is 3.8 mm using FBP and 2.7 mm using EM with automatic iteration termination [4] (9 iterations in this case).

To evaluate the spatial resolution imaging performance, images of mini Derenzo phantoms have been obtained with both modalities. Fig. 2 shows the corresponding images. In PET mode (left image) the phantom has 3.0, 2.5, 2.0 and 1.5 mm rods, while the SPECT phantom (right) also includes 1.2 mm rods.

2.2. Sensitivity

The PET absolute sensitivity has been evaluated using a \(^{22}\)Na source of about 100 kBq. The maximum sensitivity, measured at CFOV is about 2.3% with an energy window of 50–850 keV and 1.1% using 50–450 keV energy window. The PET system sensitivity has been measured with a linear source placed inside a metal tubes. The measure is repeated five times with increasing wall thickness. The system sensitivity, averaged over the whole axial FOV, extrapolated from the accumulated sleeve measurements, is 1.1%.

In SPECT mode we have evaluated the sensitivity using a glass capillary filled with about 37 MBq. The measured sensitivity is constant over the whole FOV and is about 37 cps/MBq.

2.3. Count rate

The exact methodology for measuring the scatter fraction in small animal scanners is still an open question. Here we have used the preliminary standards proposed by the small animal PET NEMA task force [3]. A phantom that mimics the body of a small mouse was scanned to estimate both the amount of measured scattered radiation and noise equivalent count rate (NEC). The phantom consists in a Lucite cylinder with 2.5 cm diameter, 7.0 cm long, with a 2 mm diameter hole drilled parallel to the central axis at a radial distance of 1 cm and filled with a known quantity of activity of a \(^{18}\)F solution. The scatter fraction has been extracted from a low activity measurement (random rate 0.2%, dead time loss <5%). Using the 50–850 keV energy window we have measured a scatter fraction (SF) of 21.7%. The NEC curve were calculated from measured true \((R_{true})\), scatter \((R_{scatter})\) and random \((R_{rand})\) rates by using the formulas: \(R_{scatter} = (R_{TOT} - R_{rand}) \times (SF)\); \(R_{true} = (R_{TOT} - R_{rand}) \times (1-SF)\); \(R_{true}/R_{TOT} = R_{true} / (R_{true} + R_{rand} + R_{scatter})\). With the pile-up rejection enabled, the energy window of 50–850 keV, in combination with a 14 ns timing window, provides a peak NEC of about 30 kcps at an activity of about 20 MBq (Fig. 3). In this condition the dead time loss is 13% while the pile-up loss is 40%. Switching off the pile-up rejection the maximum count rate is 180 kcps and the peak NEC is about 50 kcps.

2.4. Image quality

In order to evaluate the imaging performance and to compare image quality of PET and SPECT we have scanned the same object with both modalities. We have used the image quality phantom proposed by NEMA for small animal PET. The phantom drawing and resulting images are reported in Fig. 4.
3. SPECT application in neuroscience with $^{123}$I

$^{123}$I-FP-CIT (DaTSCAN) is a SPECT marker of nigrostriatal neuronal integrity, allowing differentiation of neurodegenerative parkinsonian syndromes. A new model of Parkinson disease has recently been developed by a mutation of transcription factors Engrailed-1 and Engrailed-2 which are known to play an important role in the development and maintenance of embryonic mesencephalic and adult DA neurons. The $\text{En1}^+/-/\text{En2}^-/-$ mice ($\text{EnHT}$) show a progressive degeneration of DA neurons selective for the neurons located in the Substantia Nigra during the first three postnatal months. This specific loss results in a reduced storage and release of dopamine in the caudate putamen and in a reduction of motor performances with advancement of age, reminiscent of the motor deficits observed in Parkinson’s disease.

To confirm and extend the previous analysis on the EnHT mice as a new model for Parkinson’s disease we evaluated the binding of DaTSCAN as indicator of integrity of dopaminergic system in asymptomatic EnHT mice by the small animal scanner YAP-(S)PET.

3.1. Method

SPECT image was collected 4 h after tail-vein injection of about 80 MBq of $^{123}$I-FP-CIT. Animals were pre-treated with potassium perchlorate (thyroid block) and anesthetized by intraperitoneal injection of a mix of ketamine and xylazine (60 and 4.4 mg/kg, respectively) or pentobarbital alone (50 mg/kg) for images acquisition. Images were reconstructed with EM using a dedicated procedure for $^{123}$I. Upon completion of imaging, the mice was euthanized with a lethal dose of either ketamine and xylazine or pentobarbital. Animal tissues was dissected, weighed, and then counted in a Cobra single-well-counter (Packard). Weighed standards of the injected dose were also counted.
Radiotracer biodistribution data are expressed in units of percentage injected dose per gram of tissue at the time of sacrifice for each animal. Separate samples of basal nuclei was processed to obtain ex vivo autoradiographic images with Cyclone Storage Phosphor System (Packard).

3.2. Results

Results showed a good visualization of DaTSCAN binding in basal nuclei (Fig. 5) demonstrating that YAP-(S)PET is capable of accurate and repeatable measuring DAT binding sites in the mouse brain.

4. Conclusions

The YAP-(S)PET has been fully characterized following the most recent NEMA standards. Images of a mini Derenzo phantom, showing 1.5 mm hot rods in PET mode and 2.5 mm in SPECT mode have been obtained. Imaging of a NEMA small animal phantom shows similar image quality for PET and SPECT modalities.

123FP-CIT uptake in the site of basal nuclei was confirmed by ex vivo counting as well as by autoradiographic images. The evaluation of different degree of Parkinson manifestation in EnHT mice is under investigation.

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