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PET Performance Evaluation of an MR-Compatible PET Insert

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Abstract

A magnetic resonance (MR) compatible positron emission tomography (PET) insert has been developed in our laboratory for simultaneous small animal PET/MR imaging. This system is based on lutetium oxyorthosilicate (LSO) scintillator arrays with position-sensitive avalanche photodiode (PSAPD) photodetectors. The PET performance of this insert has been measured. The average reconstructed image spatial resolution was 1.51 mm. The sensitivity at the center of the field of view (CFOV) was 0.35%, which is comparable to the simulation predictions of 0.40%. The average photopeak energy resolution was 25%. The scatter fraction inside the MRI scanner with a line source was 12% (with a mouse-sized phantom and standard 35 mm Bruker 1H RF coil), 7% (with RF coil only) and 5% (without phantom or RF coil) for an energy window of 350–650 keV. The front-end electronics had a dead time of 390 ns, and a trigger extension dead time of 7.32 μ s that degraded counting rate performance for injected doses above ~ 0.75 mCi (28 MBq). The peak noise-equivalent count rate (NECR) of 1.27 kcps was achieved at 290 μ Ci (10.7 MBq). The system showed good imaging performance inside a 7-T animal MRI system; however improvements in data acquisition electronics and reduction of the coincidence timing window are needed to realize improved NECR performance.

Index Terms

Avalanche photodiodes; positron emission tomography (PET); magnetic resonance imaging (MRI)

I. Introduction

Positron emission tomography (PET) and magnetic resonance imaging (MRI) are two complementary imaging modalities. PET provides high sensitivity *in vivo* functional imaging, while MRI provides high resolution anatomical information and also functional and biochemical information with functional MRI (fMRI) and MR spectroscopy, respectively. Simultaneous PET/MR is a promising dual-modality imaging approach for biomedical studies, both for clinical research and small animal studies.

Several laboratories have investigated the development of combined PET/MRI scanners. Different approaches that have been proposed include using light guides [1,2] or long optical fibers [3,4] to transmit scintillation light to photomultiplier tubes (PMTs) outside the magnet, split magnet designs [5], and field-cycled MRI systems [6].

Avalanche photodiodes (APD) are photodetectors that are intrinsically insensitive to magnetic fields [7], so they can be used inside an MRI scanner. MR-compatible PET scanners based on APDs or position-sensitive APDs (PSAPD) have been built for animal studies [8–10].

An MR compatible PET insert (Fig. 1) has been developed in our laboratory for simultaneous small animal PET/MR imaging [11]. This earlier paper examined the interference between the PET and MR systems and demonstrated first *in vivo* studies. The purpose of this current work was to study the detailed performance of the PET system in the MRI scanner, with the goal of identifying limitations and challenges for a second generation system that is currently being designed.

Some characteristics of this PET system are listed in Table I. The system used lutetium oxyorthosilicate (LSO) as the scintillator and position-sensitive avalanche photodiodes (PSAPD) [12] as the photodetectors. Short-length optical fiber bundles with radii of curvature from 6 to 16 mm and length of 100 mm were used to place the PET front-end electronics outside the MR field of view (FOV), as shown in Fig. 2. The benefits and effects of this optical fiber coupling were discussed in [8]. The 16 detector modules making up the system were interleaved such that 8 modules are read out at each end. Two layers of 17.5- μm thick copper shielding were placed around the PSAPDs and preamplifier electronics (AMP in Fig. 2.) to reduce the radiofrequency (RF) interference between PET and MR. The PET system used off-the-shelf Nuclear Instrumentation Module (NIM)-based electronics and a dedicated multiplexer [13] to reduce the number of data acquisition (DAQ) channels. The signals were sampled and digitalized by two multi-channel DAQ boards [14]. The data were processed with Matlab and reconstructed with filtered backprojection (FBP) or a maximum a posteriori (MAP) algorithm [15].

For combined PET/MRI studies, the insert was placed inside a 7-T Bruker Biospec small animal scanner equipped with a 120 mm inner diameter gradient set. Although the electronic transaxial FOV of the PET insert is 60 mm, it is physically limited by the diameter of the standard Bruker 1H birdcage RF coil to 35 mm.

II. Methods

PSAPD ($14 \times 14 \text{ mm}^2$ active area) and crystal array (8×8 LSO elements) were used in each detector in the system. To process the data, all events must be assigned to crystal pairs. The raw data was acquired with DAQ boards and the flood histograms (2D map of interaction position) were generated with the energy signals from the PSAPD. The peak positions (representing individual crystals) were identified in the flood histograms and crystal lookup tables (LUTs) were created using a watershed method. The events were assigned to crystal pairs based on the detector module number and the LUTs.

The energy windows were applied in two steps. One step was the hardware trigger set in the constant fraction discriminator (CFD) and the other one was applied in data processing which was done in Matlab. To obtain the energy window settings, the raw data was acquired with the CFD threshold set just above the noise, then the energy spectra were generated and the window corresponding to 350–650 keV determined for each crystal. In each detector module, the lowest amplitude corresponding to an energy of 350 keV was selected and the CFD threshold was set just below that value to minimize dead time and random events. Data was then processed in software setting energy windows of 350–650 keV for each individual crystal.

A. Energy resolution

A cylindrical phantom with inner diameter of 50 mm and length of 25 mm, filled with 100 μCi (3.7 MBq) ^{18}F -fluorodeoxyglucose (FDG) was placed in the FOV. Data were acquired for 5 minutes under four different conditions: 1) without any MR sequence, 2) with rapid acquisition with relaxation enhancement (RARE) sequence (echo time $\text{TE}=15$ ms, repetition time $\text{TR}=1000$ ms), 3) with spin echo (SE) sequence ($\text{TE}=45$ ms, $\text{TR}=1400$ ms) and 4) with fast low-angle shot (FLASH) sequence ($\text{TE}=4$ ms, $\text{TR}=155$ ms). List mode events were assigned to each crystal, the energy spectra were generated and the full width half maximum (FWHM) energy resolutions were calculated. For the energy resolution measurement, the hardware thresholds were set just below the lowest amplitudes corresponding to energy of 350 keV in each module, but no software energy windows were applied, while for all other measurements, the software energy windows were set at 350–650 keV.

B. Sensitivity

The PET insert was placed inside the MRI scanner but no MR sequence was running. A ^{22}Na point source (diameter of 0.5 mm), embedded in plastic and with an activity of 0.64 μCi (23.7 kBq) was placed at the center of the FOV (CFOV) and data acquired for 15 minutes with an energy window of 350–650 keV. A LSO background scan was also acquired for 15 minutes and subtracted from the point source count rate. The branching ratio of 0.90 was accounted for in the sensitivity calculation.

C. Scatter fraction

A line source with inner diameter of 1.0 mm, outer diameter of 1.5 mm and length of 70 mm, was filled with 35 μCi (1.295 MBq) of ^{18}F -FDG. The line source was placed in a small plastic cylinder, representative of a mouse. This cylinder was made of plexiglass (density of 1.19 g/cm³), had an outer diameter of 25.4 mm, length of 70 mm and a hole along the axial direction at 10 mm off center, holding the line source. The PET insert was placed inside the MRI scanner and data were taken under three conditions: 1) the line source was placed in the phantom, the phantom was placed in a RF coil and the coil was placed in the PET insert, 2) the line source was placed in the RF coil and the coil was placed in the PET insert, 3) only the line source was placed in the PET insert. In all three conditions, the line source was aligned along the axial direction and kept at the same position. List mode data were binned into sinograms and summed along the axial direction, then sinograms were aligned and summed for all angles, and the scatter fractions were computed. Events which are more than 17.5 mm away from the center were set to zero. Region within ± 5 mm of the center (after aligning all projections) were chosen to cover the line peak and the average value of left and right margin bins was assumed to be average scatter portion inside the region [16].

D. Count rate performance

There are two basic dead time models [17], non-paralyzable and paralyzable which are described by Eqs. (1) and (2) respectively, where m is the observed count rate, n is the true count rate and τ is the dead time.

$$m = \frac{n}{1 + n \times \tau} \quad (1)$$

$$m = n \times e^{-n\tau} \quad (2)$$

To measure the dead time and the count rate performance, decay experiments are commonly used [17]. In the decay experiment, the true count rate n decays exponentially as described by Eq. (3) where t is the time, n_0 is the initial count rate at time 0, and λ is the decay constant.

$$n = n_0 \times e^{-\lambda t} \quad (3)$$

The initial count rate is usually unknown, while t and m can be measured. Substituting Eq. (3) into Eqs. (1) and (2) results in Eqs. (4) and (5) respectively. For non-paralyzable dead time, a plot of $me^{\lambda t}$ versus m can be fitted to a straight line with an intercept of n_0 and a slope of $-n_0\tau$. For paralyzable dead time, plotting $\lambda t + \ln m$ versus $e^{-\lambda t}$ and fitting to a line, gives an intercept of $\ln n_0$ and a slope of $-n_0\tau$. Therefore, τ can be calculated [17].

$$me^{\lambda t} = -n_0\tau m + n_0 \quad (4)$$

$$\lambda t + \ln m = -n_0\tau e^{-\lambda t} + \ln n_0 \quad (5)$$

The trigger processing diagram for the current PET insert is shown in Fig. 3. The 16 modules were divided into four groups, for each group all signals were ORed together, and coincidences were generated from these 4 groups. A trigger extension module (Ext in Fig. 3) was needed prior to the DAQ to ensure proper synchronization of the two DAQ boards in the system. Triggers were extended to give a total duration of 8.09 μ s.

To measure the count rate performance, a cylindrical mouse-sized phantom with inner diameter of 25.4 mm and length of 70 mm was filled with water containing 1.21 mCi (44.77 MBq) ^{18}F -FDG. The phantom was placed in the RF coil and the coil was placed at the center of the FOV. The PET insert was placed inside the MRI scanner with no MR sequence running (The effect of MR sequences are discussed in the discussion section). The single event count rates of the 4 detector groups, coincidence count rates, and the count rates before and after the trigger extension modules were recorded every 15 minutes. Data were taken over 5 half-lives. The single event count rates were fit to a paralyzable model and front-end dead time was calculated. The count rates before versus after the trigger extension module were fit to a paralyzable model and the dead time of the trigger extension module was calculated.

To calculate the noise equivalent count rate (NECR), the random rates should be measured. There are two methods to measure the random rates. One is the delayed method and the other is based on measuring the single rates [18]. The present system used a wide coincidence window (80 ns) because of the position-dependent timing delays caused by the resistive readout of the PSAPDs [8]. This makes it difficult to apply the delayed window method with a coincidence logic unit. Therefore, the single event count rates of the four detector groups were recorded and the random rates were calculated from the single rates.

The NECR was calculated using Eq. (6), where R was the random rates which were calculated from single rates, k was the fraction of transaxial FOV occupied by the phantom (0.423 in this measurement), and true (T) and scatter (S) rates are defined in Eqs. (7) and (8) respectively. In Eqs. (7) and (8), the prompt (P) rate was the directly measured and scatter fraction (SF) was taken from the scatter fraction measurement for the line source inside the phantom, with the phantom inside the RF coil.

$$NECR = \frac{T^2}{T + S + kR} \quad (6)$$

$$T = (P - R) \times (1 - SF) \quad (7)$$

$$S = (P - R) \times SF \quad (8)$$

E. Reconstructed image spatial resolution

A plastic holder with three line sources (inner diameter of 0.68 mm, outer diameter of 1.2 mm and length of 80 mm) was filled with a total of 40 μCi (1.48 MBq) ^{18}F -FDG. The three line sources were located at the center and at radial positions of 5 mm and 10 mm. Data were acquired for 5 to 10 minutes (depending on activity concentration) under different conditions: without any MR sequence, and with RARE, SE and FLASH sequences. Six data sets were taken for each condition.

The normalization scan was acquired with a cylindrical phantom with inner diameter of 50 mm and length of 25 mm, filled with ^{18}F -FDG covering the whole useful FOV. The sinogram was generated and the efficiency of each detector element was calculated by summing all lines-of-response (LOR) containing that detector element. The normalization factor of each LOR was computed using the product of the detection efficiencies of the two detector elements forming the LOR. For FBP reconstruction, the normalization was directly applied to the emission sinograms.

Sinograms were generated, then normalized and rebinned with single-slice rebinning (SSRB). The slice thickness was 0.75 mm. Images were reconstructed with 2-D FBP using a Shepp-Logan filter with a cut-off frequency of 1.0. Profiles of central slices of images along the radial and tangential direction were plotted and fit with a Gaussian. The FWHM was calculated.

F. Phantom study

An ultra-micro hot spot phantom (Data Spectrum Corporation, Hillsborough, NC, USA) was filled with 60 μCi (2.22 MBq) ^{18}F -FDG and scanned for 2 hours. Data were acquired and processed. Sinograms were generated, then normalized and rebinned with SSRB. The thickness of slice was 0.75 mm. Images were reconstructed with FBP using a Shepp-Logan filter with a cut-off frequency at the Nyquist frequency.

The same data set also was reconstructed with 3-D MAP. Normalization was incorporated into the forward model in MAP reconstruction and no attenuation correction was applied. The number of iterations of MAP reconstruction was 30 and the regularization parameter β was 10^{-6} . The image size was $101 \times 101 \times 17$ and the voxel size was $0.35 \times 0.35 \times 0.75 \text{ mm}^3$. The central slice of image was chosen and compared with the same slice from FBP.

III. Results

A. Energy resolution

The flood histogram from one detector module inside the MRI scanner (no MR sequence running) is shown in Fig. 4 (left). All crystals were resolved. The observed pincushion distortion was due to the resistive readout of PSAPD and the rotation was due to the static magnetic field altering the charge collection in the PSAPD. These were not issues as long as all crystals could be identified, but the compensation, either optimized resistive layer [19] or post processing [20,21], would help to ease the flood histogram segmentation. The energy spectra from four representative crystals are shown. No obvious difference in flood histograms or energy spectra was observed with and without MR sequences. The energy resolutions were 22%, 24%, 26% and 25% respectively for the four crystals. The energy resolution histogram is plotted in Fig. 5. The average energy resolution of the overall system was 25% with a minimum of 17% and maximum of 43%. The standard deviation was 5.5%.

B. Sensitivity

With the energy window of 350–650 keV, the sensitivity measured with ^{22}Na at the center of the FOV inside the MRI scanner, but without any MR sequence running, was 0.35%, which is comparable to the GATE [22] simulation result of 0.40%.

C. Scatter fraction

Sinograms were generated from the line source data, aligned and all projection angles were summed. The profiles are shown in Fig. 6. The scatter fractions calculated were 12%, 7% and 5% for the phantom and RF coil, RF coil only and with neither phantom nor RF coil, respectively.

The results show that the contribution of the PET insert supporting materials and the MRI scanner to scatter is similar to that of the mouse-sized phantom (~5%). The RF coil contributes less (~2%).

D. Count rate performance

The single event count rates of one detector group are plotted against the activity, and fit to a paralyzable dead time model (Figs. 7a and 7b). The points are the measured data points and the solid line is the fit. The dead time calculated was 390 ns. Only small dead time effects (less than 7% single event loss or less than 14% coincidence event loss) were observed for an activity of 1 mCi (37 MBq) (approximately five times the standard injected dose for a mouse). However, the shaped energy signals are much slower (~1 μs) than the timing signal, so the actual count rate is limited more by pile-up, which causes mispositioning and an energy offset.

The count rates before versus after the trigger extension module are plotted in Fig. 7c and fit to a paralyzable dead time model (Fig. 7d). The points are the measured data and the line is the fit. The calculated dead time of the trigger extension module is 7.32 μs .

The prompt rates (solid line with plus sign), random rates (solid line with circle) and true rates (dashed line) for a cylindrical phantom were measured as a function of activity and are plotted in Fig. 8. The random rates were calculated with timing window of 80 ns. These random events include all possible LORs. The NECR (solid line) is also plotted in Fig. 8 (scale on the right). The scatter fraction was 12% with the phantom and RF coil, k was 0.423, calculated using the phantom diameter of 25.4 mm and the electronic transaxial FOV of 60 mm. The peak NECR of 1.27 kcps was achieved at 290 μCi (10.7 MBq).

E. Reconstructed image spatial resolution

The reconstructed radial and tangential image spatial resolution without any MR sequence running, and with RARE, SE and FLASH sequences, are shown in Table II. The standard deviations were calculated from the 6 repeated experiments. This data demonstrates that the MR sequences had almost no effect on spatial resolution. The average of these three locations' reconstructed spatial resolution was 1.51 mm.

F. Phantom study

The ultra-micro hot spot phantom image was reconstructed with FBP and MAP algorithms. The central slices of images are shown in Fig. 9. With FBP reconstruction, the 1.7-mm rods can be clearly resolved and the 1.35-mm rods can be resolved with careful inspection. This data further supports the resolution data in Table II. With MAP reconstruction, the 1.35-mm rods can be clearly resolved and the image has fewer artifacts as anticipated.

IV. Discussion

The variations in energy resolution are primarily due to the optical fiber bundle [8] and the non-uniformity of gain of the PSAPD. The PSAPDs were divided into two groups, and the same high voltage was applied to each group. Each PSAPD has its own unique gain-voltage characteristics, and thus has a different gain at the same high voltage.

To compare our MR-compatible PET insert with other small animal PET systems, the sensitivity, spatial resolution and NECR are listed in Table III for several microPET scanners [23–26]. The spatial resolution is the average value in the radial and tangential directions. The spatial resolution of this insert is competitive with the first generation microPET prototype [18] and is not affected by the MR system.

The sensitivity is however significantly lower than microPET R4 [24] and microPET Focus-F120 [26]. Improved sensitivity can be realized by adding more detector rings axially and/or increasing scintillator length. It should be noted that increasing length may require design to deal with depth-of-interaction (DOI) effect [27]. GATE Monte Carlo simulations suggest that the sensitivity increases to ~1.6% at the CFOV with 4 rings of the same detectors, and to ~6.8% with 4 rings of longer (18 mm long) detectors with the same ring diameter.

The sensitivity measurement and the count rate performance were taken inside the MRI scanner without running any MR sequence. The MR sequences have very small (and not statistically significant) effects on the count rate or sensitivity of the PET system [11]. These effects may be attributed to interference from RF pulses and rapid gradient switching. The ratio of count increase/loss is related to RF power or the gradient strength/switching time and duty cycle of the sequence and therefore depends on the exact sequence. The detailed reasons and solution are still under investigation; however for pulse sequences studied to date, the counting rate and sensitivity are changed by less than 2%, even when running RF or applying gradients at maximum power.

Dead time components of the current DAQ system have been measured, and the NECR was measured with a mouse-sized phantom. Compared with microPET systems, the NECR peaks at lower activity and the peak value is lower. It peaks at 290 μCi (10.7 MBq), which is close to the optimal injected dose for a mouse (typically 100–200 μCi or 3.7–7.4 MBq). For the original microPET scanner, the NECR was around 2 kcps for the same activity of 290 μCi (10.7 MBq) at a concentration of 0.049 MBq/cc in a phantom volume of 220 mL or around 4.5 kcps at a concentration of 0.093 MBq/cc in a phantom volume of 115 mL [23].

The NECR is fairly low because of the wide coincidence window on the current system. It will be dramatically improved in the next generation when upgraded coincidence trigger electronics including crystal-dependent timing shifts will be implemented to account for position-dependent time delays due to the resistive readout of the PSAPDs. This will allow a much narrower coincidence window (~ 12 ns) to be used. The NECR is also expected to vary very slightly with MR pulse sequence, due to the small effects on the counting rate described above. As the effects are smaller than a 2% change in the prompt counting rate, no significant change in the NECR is expected.

One point to note is that on this system, the rates of random coincidence events are estimated from the measured single event rates. However, this slightly overestimates the random rates, as the single event rates also includes single events that result in true coincidence events [28]. Furthermore, the true rates are computed by subtracting the estimated random rates from the measured prompt rates, and therefore an overestimation of the random rates leads to an underestimation of the true rates. The effect of these errors can be estimated by a two-step process in which the random rates are recalculated by using the single rates with the estimated true rates subtracted. At an activity of 290 μCi (10.7 MBq), the overestimation of the random rate was $\sim 5\%$, the underestimation of true rate was $\sim 9\%$ leading to an estimated underestimation of NECR of $\sim 16\%$. However, this correction was not applied to the data presented in Fig. 8 as the methodology is yet to be widely accepted, and we therefore prefer to report the more conservative results obtained using conventional NECR calculation.

V. Conclusions and Future Work

These measurements show that the MR-compatible PET insert has good performance inside the MR system when running typical pulse sequences. Overall, the performance of this PET insert is comparable to that of first generation small animal PET systems and therefore is sufficiently good for a wide range of biologically relevant studies, with the advantage of being able to acquire MR data simultaneously. The insert is now being used for a range of mouse studies, while a second generation prototype that significantly improves sensitivity, NECR and axial field of view is under development.

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Fig. 1.
Photograph of MR-compatible PET insert sitting in the MRI scanner.

Fig. 2.
Schematic cross-sectional view of the PET insert in the MRI scanner.

Fig. 3.
Trigger processing diagram.

Fig. 4.
Flood histogram (left) and representative energy spectra (right).

Fig. 5.
Distribution of energy resolution values for each detector element in the system.

Fig. 6. Scatter profiles: with phantom and RF coil (solid line), with RF coil only (dashed line) and with neither phantom nor RF coil (dotted line).

Fig. 7.
Count rates and fitting. See text for details.

Fig. 8.
Count rates: prompt, random, true rates and NECR vs. activity.

Fig. 9.
Ultra-micro hot spot phantom image reconstructed with FBP (left) and MAP (right).

TABLE I

Characteristics of PET System

Characteristic	Value
Number of modules	16
Ring diameter	60 mm
Axial field of view	12 mm
Transaxial field of view	35 mm
Number of crystals	1024
Crystal size	1.43×1.43×6 mm ³
Insert length	550 mm
Insert outer diameter	118 mm

TABLE II

Reconstructed Spatial Resolution (mm)

	No Seq.	RARE	SE	FLASH
Center	Radial	1.34±0.05	1.30±0.04	1.31±0.02
	Tang.	1.13±0.06	1.13±0.06	1.11±0.05
5 mm	Radial	1.74±0.03	1.73±0.02	1.72±0.03
	Tang.	1.58±0.02	1.62±0.04	1.60±0.04
10 mm	Radial	1.60±0.03	1.57±0.05	1.56±0.03
	Tang.	1.72±0.06	1.72±0.06	1.69±0.05

TABLE III

Sensitivity, Spatial Resolution and NECR of Several PET Systems

	Energy Window	Timing Window	Sensitivity at CFOV	Spat. Res. at CFOV	Phantom Size (Diameter, Length)	Peak NECR@ activity
microPET [23]	250–650 keV	12 ns	0.56%	1.7 mm	50.8 mm, 108.5 mm	4.1 keps @ 1.76 mCi (65.1 MBq)
	350–650 keV	12 ns	0.4%			
microPET R4 [24]	250–750 keV	6 ns	4.37%		43 mm, 76 mm	174 keps @ 2.08 mCi (77 MBq)
	350–750 keV	6 ns		1.65 mm	43 mm, 76 mm	168 keps @ 2.46 mCi (91 MBq)
	350–650 keV	6 ns	2.45%			
microPET Focus 120 [25]	250–750 keV	6 ns	6.7%	1.34 mm	25 mm, 70 mm	809 keps @ 2.4 mCi (88 MBq)
	350–650 keV	6 ns	4.4%		25 mm, 70 mm	~760 keps @ ~2.7 mCi (~100 MBq)
microPET Focus 120 [26]	250–750 keV	6 ns	6.7%	1.15 mm	30 mm, 70 mm	869 keps @ 4.34 mCi (160.58 MBq)
	350–650 keV	6 ns	3.8%		30 mm, 70 mm	741 keps @ 4.00 mCi (147.90 MBq)
this PET insert	350–650 keV	80 ns	0.31%	1.21 mm	25.4mm, 70 mm	1.27 keps @ 290 μ Ci (10.7 MBq)