Development and Performance Evaluation of a High-Sensitivity Positron Emission Tomography Scanner Dedicated for Small-Animal Imaging

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Abstract—Developing a dedicated small-animal positron emission tomography ($\mu$PET) system of high sensitivity presents an important challenge. To address this challenge, we investigate a non-conventional design strategy for developing PET systems in which the hardware and software components of the system are synergistically combined in such a way that the certain limitations of the hardware design are overcome by reconstruction. Employing this design concept, we develop a prototype that employs two off-the-shelf detector panels having large area and high intrinsic detection efficiency in a compact geometry for achieving high sensitivity. Resolution degradations associated with the compact scanner design, on the other hand, is corrected for by using an well-established image reconstruction algorithm. We show that our prototype can generate a central sensitivity of $\sim 30\%$ and an image resolution of $\sim 1.2\, \text{mm}$. Over the typical ranges of radioactivity currently used for conducting FDG-PET imaging of rodents, the prototype has an acceptable count-rate capability and provides a noise-equivalent count rate significantly higher than those of other $\mu$PET systems reported in the literature. The prototype therefore demonstrates that the development of a high-sensitivity $\mu$PET scanner is already within the reach of current PET technologies if this non-conventional synergistic design strategy can be adopted.

Index Terms—positron emission tomography, small-animal PET, high-sensitivity, synergistic design

I. INTRODUCTION

A S positron emission tomography (PET) finds wider use in clinic and research, there arises the need for higher standards on its imaging performance and, at the same time, growing pressure for improving the cost effectiveness of the instrument. To date, PET image resolution has been significantly improved to reach the sub-millimeter level for imaging small animals, mostly through advances made to the detector technologies [1]–[6]. In contrast, the sensitivity of current clinical and small-animal PET ($\mu$PET) systems remains quite low, typically below 5% [5]–[7]. The need for high sensitivity is not difficult to observe. When using the same amount of radioactivity and imaging time, more sensitive PET systems can generate images having higher signal-to-noise ratios (SNRs) for improving the detection of abnormalities/changes and the accuracy in quantification [5,6]. Conversely, to achieve a certain image SNR, more sensitive PET systems allow one to use lower radioactivities for reducing the radiation dose to subject, or to use shorter imaging time for increasing the imaging throughput or the temporal resolution in dynamic studies (which in turn can result in quantitatively more accurate biokinetic parameters). Also, many applications critically require high sensitivity because the signals of interest can be inherently limited in strength. For example, the signal in neuroreceptor imaging can be limited by the number of binding sites available, as well as the specificity and affinity of the radiotracers [8]. Similarly, the number of foreign cells that can be used in cell-trafficking studies can be limited and long tracking time to follow the cells is often necessary [9].

Sensitivity is a particularly important concern in $\mu$PET imaging. In order to maintain the quantitative accuracy per image voxel under similar imaging conditions, the volumetric resolution and sensitivity need to be improved by the same amount [5,6]. In comparison with clinical PET imaging, $\mu$PET imaging has now achieved better than 300-fold increase in the volumetric resolution; however, their sensitivity is only comparable [5]–[7]. This inadequate sensitivity found with current $\mu$PET imaging can be compensated for to some extent by use of long imaging time and high radioactivity concentrations. However, at present the amount of radiotracer used in a typical $\mu$PET imaging protocol can yield a radiation dose ten times that in clinical PET imaging, giving rise to serious concerns for the radiobiological effects in current $\mu$PET studies [6,10].

Developing an affordable $\mu$PET scanner to provide a level of sensitivity and resolution desired for $\mu$PET imaging is of great significance. Feasible approaches for implementing scanners of this kind are yet to be demonstrated. We have previously reported that one promising approach is to employ an opposing pair of large-area detectors capable of certain depth-of-interaction (DOI) resolution with a tight detector spacing [11]. In this paper, we describe a prototype that adopts this compact, dual-head design and report the performance properties obtained for this scanner by measurements and simulations. Our results show that the prototype can yield a central sensitivity of $\sim 30\%$ and an isotropic image resolution of $\sim 1.2\, \text{mm}$. Additionally, the prototype assumes a stationary configuration and can provide an image field-of-view (FOV) of $25 \times 17 \times 5\, \text{cm}^3$ to accommodate an entire rodent (or multiple rodents). The scanner’s high sensitivity and large FOV make it particularly useful for monitoring the spatio-temporal
distributions of radiotracers at high temporal resolutions and over long periods of time.

The rest of this paper is organized as follows. In Sect. II, we describe the design of the dual-head \( \mu \)PET prototype and discuss important considerations in adopting this design. In Sect. III, we report the sensitivities and noise-equivalent count rates obtained for the prototype by measurements and Monte-Carlo simulations. We also show some real-data images obtained for a spinal needle, a resolution phantom, and a healthy rat. Finally, concluding remarks are given in Sect. IV.

II. DESIGN CONSIDERATIONS AND THE PROTOTYPE

A. Considerations for high-sensitivity \( \mu \)PET systems

As mentioned above, the sensitivity of current \( \mu \)PET imaging needs to be substantially increased. This task appears simple: to build a scanner that has a high geometric efficiency (GE) to intercept most gamma-ray photons originating inside the volume of interest, and a high detector efficiency (DE) to register the intercepted photons. As we will discuss below, this task turns out to be quite challenging.

1) Considerations for increasing GE: To obtain high GE, one needs large detection solid-angles (DSAs) and dense detector packing. Given the same amount of detectors, more compact scanner geometries yield detection surfaces covering larger DSAs. For covering a given detection surface, the use of large-area detector panels (called detector plates below) can reduce detector gaps and yield dense packing. Cost-effective designs have been proposed for building detector plates (such as the quadrant-sharing configuration [12]) and many new technologies under examination naturally lead to the plate geometry [13]–[16]. The use of detector plates also yields an extended scanner AFOV. A large AFOV means a reduced number of bed position for imaging a subject, making the scanner more suitable for monitor the spatial-temporal variations of a radiotracer inside a subject. It is also noted that the sensitivity of a scanner decreases from a maximum at the center (which is the central sensitivity commonly reported for a \( \mu \)PET scanner) to zero at the edges of the AFOV. Therefore, given two scanners having the same central sensitivity, the longer one can provide a considerably higher sensitivity to (more uniform noise distributions within) a subject because the average sensitivity to the subject volume is higher (the sensitivity variations within the volume is smaller). Consequently, the gain in subject sensitivity provided by a larger-AFOV scanner over a smaller-AFOV scanner can be considerably higher than suggested by their reported central sensitivity. These considerations for the sensitivity, cost effectiveness, and technology trend have motivated us to examine the use of the detector plates for building high-sensitivity \( \mu \)PET systems.

There is a fundamental challenge associated with increasing the GE, however. To first order, the true event-rate (i.e., the sensitivity) increases linearly with the GE, but the scatter and random event-rates increase quadratically [17,18]. As a result, increasing the GE does not necessarily improves the net sensitivity of a PET scanner, which is often measured by the noise-equivalent count rate (NECR). Fortunately, in \( \mu \)PET imaging the concern for elevated scatter and randoms with a large GE is greatly alleviated by the nature of the imaging task: the subject is small (thus reduced scatter) and the amount of radiotracer administrated is low (thus reduced randoms).

2) Considerations for increasing DE: To obtain high DEs, the detectors shall employ thick, high-density scintillators, e.g., 20-30 mm long LSO crystals to provide 2.30-3.45 attenuation lengths for 511 keV photons. For \( \mu \)PET imaging, the detector also needs to use narrow crystals for providing high intrinsic spatial resolution. A 1.2 mm image resolution is useful for many applications in \( \mu \)PET imaging, but a higher resolution is welcome. Based on our empirical observations with existing \( \mu \)PET systems [5,6,19]–[21], this resolution would require the use of ~1.2 mm width, or narrower, crystals. Using thick and narrow detectors in a compact scanner configuration is the recipe for producing pronounced depth-of-interaction (DOI) blurs that will severely degrade the image resolution. Consequently, the detectors shall have adequate DOI capability as well. Ideally, the DOI resolution needs to be comparable with the crystal width so that the apparent aperture of the crystal does not show significant changes as the incident angle of the gamma ray varies. The negative impacts of DOI blurs to PET image quality have been widely recognized [5,6] and the development of DOI detectors is an important and active field of research [15,22]–[31]. At present, mature technologies to produce in large quantity, and at affordable cost, detectors that can provide 2-3 attenuation lengths (or longer) for 511 keV gamma rays. 1.2 mm intrinsic resolution (or better), and ~1-3 mm DOI resolution are not available.

3) Other practical considerations: Due to cost consideration and theoretical interest, we are interested in using only two detector plates and adopting a stationary geometry. This scanner configuration has the following practical advantages. First, the mechanic design for a stationary, dual-head scanner is quite simple and there is no need for maintaining the mechanical alignment during detector motion. Second, detector motion introduces additional complexity in reconstruction and can decrease the temporal resolution in dynamic studies. Third, subject handling is easier when the scanner stays stationary, especially when the scanner employs a compact geometry. Fourth, it allows the use of the entire space between the detectors for imaging. The dual-head geometry also allows one to readily change the detector spacing and increases the scanner’s flexibility. A stationary, dual-head scanner, however, cannot completely surround the subject and will generate incomplete data (containing missing views and projection truncations). However, the degree of incompleteness may not present critical challenge in practice.

B. A synergistic system design

The above analysis suggests that, for developing high-sensitivity \( \mu \)PET systems, presently one shall focus the effort on substantially improving the detector technologies. This conventional analysis does not take into consideration the interplay between the hardware and software components of a PET scanner, specifically the ability of advanced reconstruction methods to substantially improve the resolution and statistical quality of PET images by employing models that accurately
characterize the physical and statistical properties of the detection response of a scanner (below we refer to such methods as model-based reconstruction methods) [32,33]. This known fact indicates that data generated by the current PET systems contain more information than it is utilized for producing images. Therefore, we postulate that it is possible to develop a high-sensitivity \( \mu \)PET scanner by employing existing PET technologies if the hardware and software components of the scanner can be synergistically combined to address the current situation of under-utilization of data information.

Based on the considerations and motivations given above in Sect. II.A, we have identified the HRRT (High Resolution Research Tomograph) detector technology as one promising off-the-shelf detector technology for developing the proposed dual-head, high-sensitivity \( \mu \)PET scanner [34]–[36]. Below in Sect. II.C, we will provide a more detailed summary of the HRRT technology. Here, we note that the technology is mature, commercially available and well tested. It adopts a cost-effective design, has reasonable energy and timing resolutions, offers a large detection-sensitive area, employs thick scintillators (with respect to most other \( \mu \)PET systems), and produces binary DOI measurements. The detector, however, uses \( \sim 2.1 \) mm wide crystals (\( \sim 2.4 \) mm crystal pitch) and provides marginal resolution for \( \mu \)PET imaging. As an evidence, the HRRT system, which employs eight HRRT detectors in an octagonal geometry for imaging human brains, has an image resolution slightly worse than 2 mm [35,36]. The compact geometry of the proposed scanner will produce pronounced DOI blurs to further reduce the resolution.

1) Target sensitivity and resolution: Assuming a triangular response function for an opposing detector pair, the 2.1 mm crystal width of the HRRT detector suggests that the scanner can potentially achieve a spatial resolution having a FWHM of \( \sim 1.05 \) mm [18]. Based on the size, packing density and scintillation materials of the detector, we estimate that a dual-head scanner employing the HRRT detectors and a 5 cm detector spacing can yield a DSA that covers 80\% of the 4\( \pi \) solid-angle, and achieve a sensitivity of \( \sim 38\% \), for the point at the center of the scanner. Taking these considerations together, we therefore postulate that the proposed dual-head scanner employing the HRRT detectors and adopting a model-based reconstruction algorithm can achieve a central sensitivity of \( \sim 30\% \) and an image resolution of \( \sim 1.2 \) mm.

2) Synergistic integrations: In theory, one can target for even higher image resolution and eliminate altogether the use of DOI detectors by relying on the reconstruction process to provide aggressive corrections for the DOI blurs and other resolution degradations. An important issue of relevance here is the amplifications of data noise, modeling errors and computation errors when performing aggressive corrections. As a result, the benefits of gained sensitivity may be lost to the amplified noise and errors in the resulting images. Moreover, for performing aggressive corrections the physical and statistical responses of the systems need to be modeled with high accuracy. In practice, however, one can only expect to achieve limited modeling accuracy. Therefore, in choosing the HRRT detectors that provide a reasonable resolution and a moderate DOI resolution, we have applied the concept of synergistic integration in the sense that the degradations presented by the hardware design with respect to the performance targets are not too severe to be effectively corrected for by reconstruction.

As mentioned above, the large DSA offered by the prototype causes increased detections of scatter and randoms as well. Thus, the energy and coincidence windows also need to be synergistically determined with respect to the subject size, administrated radioactivity, and reconstruction method. At present, little information is available for guiding synergistic integrations. One important goal of this paper is to validate the synergistic system design concept by implementing and evaluating the proposed dual-head \( \mu \)PET prototype. In subsequent work, we will concern with the task of deriving systematic knowledge from working with the prototype to generate guidelines and rules for establishing the synergistic design principles.

C. The prototype

Figure 1 shows our table-top, stationary prototype that employs two HRRT detectors with a detector spacing of about 5 cm. The spatial responses of this hardware configuration have been modeled by use of Monte-Carlo (MC) simulations and employed by a model-based iterative reconstruction algorithm. Technical details of the HRRT detector, as well as the MC modeling and reconstruction algorithm, have been reported by us and others elsewhere [34]–[39]; they are summarized below for reader’s convenience.

1) HRRT detector technology: The HRRT detector head has a detection sensitive area of about 25\( \times \)17 cm\(^2\). It contains a 9\( \times \)13 array of crystal blocks, coupled to a 10\( \times \)14 array of photomultiplier (PM) tubes in a cost-effective quadrant-sharing configuration. An individual crystal block contains 8\( \times \)8 double-layered LSO/LYSO detection elements, each of which is 2.1 \( \times \) 2.1 \( \times \) 20 mm\(^3\) in size (the individual LSO and LYSO segment is 10 mm long). The crystal pitch is about 2.43 mm. The scintillation materials LSO and LYSO offer a good stopping power for 511 keV gamma rays (which translates into a high DE), high light yields (which translates into a good energy resolution), and short scintillation decay constants (which are important for achieving a good count-rate capability). The difference between the LSO and LYSO decay constants allows the electronics to determine in which crystal layer a detection event occurs, therefore yielding a DOI resolution of about 10 mm. The LSO layer is closer to the subject. The HRRT electronics allow users to apply a wide range of energy windows and provides four coincidence windows of 2 ns, 6 ns, 10 ns and 22 ns. List-mode data are generated.

2) A model-based reconstruction method: Because the HRRT detector contains two layers of 104\( \times \)72 crystals, our prototype produces a total of (2\( \times \)104\( \times \)72)\(^2\) lines of response (LORs). Also, the detection-sensitive volume between the two detectors with a 5 cm spacing is as large as 25\( \times \)17\( \times \)5 cm\(^3\). To fill this volume would require a total of 1.7\( \times \)10\(^7\) image voxels of (0.5 mm\(^3\)) in size. The dimension of the resulting reconstruction problem is tremendous, creating a substantial challenge in modeling (or measuring) and storing the spatial...
Figure 1. Our table-top, stationary prototype consists of two HRRT detectors, which have a detection active area of ~25 × 17 cm², in a compact configuration to yield a high system sensitivity. The detector spacing as shown is ~5 cm. The compact geometry leads to substantial DOI blurs, which are corrected for in reconstruction by employing an MC-generated system model that characterizes the spatial responses of the prototype.

Figure 2. The central sensitivity of the prototype estimated by using Monte-Carlo simulation. The prototype assumes a detector spacing of 5 cm, a 20% energy resolution, and a 3 ns coincidence timing resolution. The horizontal axis is the lower-level discriminator (LLD) setting of the energy window, with the upper-level discriminator fixed at 750 keV. The vertical axis is the central sensitivity in percentage. Three coincidence windows, including 2 ns, 6 ns and 10 ns, are considered. The results obtained by using the 6 ns and 10 ns coincidence windows are essentially identical.

Figure 3. Sensitivity of the prototype to a 16×8 cm² area on the midplane between the detectors at three energy windows and with a 10 ns coincidence window. Top row: measured results by using a small source filled with FDG. Bottom row: Monte-Carlo simulation results.

The cylinders were filled with FDG solution of ~5 mCi and the radioactivity of the LSO/LYSO (which are measured with a 5.4% uncertainty) was ~28.2% of the activity from the center and when reducing the EW. With the 200-750 keV EW, the measured sensitivity stays above 10% for the 16×8 cm² area examined. When using a narrower 400-750 keV EW, the sensitivity over the same area is still above 5.4%. When using the 200-750 keV EW, a central sensitivity of ~27% (obtained when using the 250-750 keV EW). Figure 3 shows the sensitivity of the prototype to an 16×8 cm² area on the midplane between the detectors, obtained by MC simulations and measurements with FDG (F-18 labeled 2-fluoro-2-deoxy-D-glucose). For the measured results, the branching fraction of the F-18 (0.98) and the event rates due to the natural radioactivity of the LSO/LYSO (which are measured with a 10-minute scan time) were corrected for. As expected, the sensitivity over the midplane decreases when moving away from the center and when reducing the EW. With the 200-750 keV EW, the measured sensitivity stays above 10% for the 16×8 cm² area examined. When using a narrower 400-750 keV EW, the sensitivity over the same area is still above 5.4%. When using the 200-750 keV EW, a central sensitivity of ~27% is measured for the prototype. This is slightly higher than the ~26.6% value obtained by simulation. Also, the measured sensitivity decreases faster than does the simulated result when moving away from the center and when reducing the EW. Here, we note that the simulated results are obtained by using an average 20% energy resolution and a 3 ns timing resolution. The HRRT detectors, however, show considerable variations in these resolutions across detection channels.

III. PERFORMANCE MEASUREMENTS

A. Sensitivity

As already mentioned above, based on the detector geometry, material and spacing, we estimate that the prototype can provide a central sensitivity of ~38%. By using a Ge-68 rod source, we measured the average energy and timing resolutions of our HRRT detector heads to be about 20% at 511 keV and 3 ns FWHM (full width at the half-maximum), respectively, which are consistent with the results reported by others [35,36]. We employed the public-domain GATE package to accurately model the configuration of the prototype, with the above-mentioned energy and timing resolutions, for estimating the scanner’s detection performance. Figure 2 shows the resulting central sensitivity obtained for various energy windows (EWs) and three coincidence windows (CWs). Our results show that there is little difference between the 6 ns- and 10 ns-CW results, and that the highest sensitivity is ~27% (obtained when using the 250-750 keV EW). Figure 3 shows the sensitivity of the prototype to an 16×8 cm² area on the midplane between the detectors, obtained by MC simulations and measurements with FDG (F-18 labeled 2-fluoro-2-deoxy-D-glucose). For the measured results, the branching fraction of the F-18 (0.98) and the event rates due to the natural radioactivity of the LSO/LYSO (which are measured with a 10-minute scan time) were corrected for. As expected, the sensitivity over the midplane decreases when moving away from the center and when reducing the EW. With the 200-750 keV EW, the measured sensitivity stays above 10% for the 16×8 cm² area examined. When using a narrower 400-750 keV EW, the sensitivity over the same area is still above 5.4%. When using the 200-750 keV EW, a central sensitivity of ~27% is measured for the prototype. This is slightly higher than the ~26.6% value obtained by simulation. Also, the measured sensitivity decreases faster than does the simulated result when moving away from the center and when reducing the EW. Here, we note that the simulated results are obtained by using an average 20% energy resolution and a 3 ns timing resolution. The HRRT detectors, however, show considerable variations in these resolutions across detection channels.

B. Noise-equivalent count rates (NECRs)

We measured the NECR curves for mouse- and rat-sized cylinders by using various EWs and CWs. The mouse-sized cylinder was 2.7 cm in diameter and 8 cm in length, yielding a volume of 45 cm³. The rat-sized cylinder was 4.6 cm in diameter and 13.5 cm in length, yielding a volume of 220 cm³. The cylinders were filled with FDG solution of ~5 mCi and the...
Figure 4. Measured count-rate curves versus the total radioactivity inside the object obtained for the mouse- and rat-sized cylinders (filled with FDG) by using three CWs, including 2 ns, 6 ns and 10 ns. Each graph contains three groups of curves obtained for the prompt (solid curves), randoms (dash curves) and total (dotted curves). The total rate is the sum of the prompt and delay rates. Each curve group contains results obtained with six EWs having the same upper-level discriminator (ULD) setting of 750 keV. Their lower-level discriminator (LLD) settings are 200 keV, 250 keV, 300 keV, 350 keV, 400 keV, and 450 keV. Within each group, the count rate decreases as the LLD increases.

Figure 4 shows the resulting count-rate curves obtained with the mouse- and rat-sized cylinders. As expected, both the prompt and delayed event rates increased as wider EWs were used. Also, the delayed event rates increased with the CW. The prompt event rates increased substantially when increasing the CW from 2 ns to 6 ns, suggesting a significant increase in the true and scatter event rates as well. In contrast, the difference in the prompt event rates obtained by using 6 ns and 10 ns CWs can be attributed to the difference in the delayed event rates, suggesting small differences in the true and scatter event rates at these two CW settings. This is consistent with the average 3 ns coincidence timing resolution measured for the prototype. It can also be observed that, depending on the EW and CW settings, the prompt event rates of the prototype saturates at a total activity of 20-50 MBq (0.54-1.62 mCi).

Figure 5 shows the NECR curves derived by applying Eq. (1) to these count-rate measurements. It is observed that the use of the 6 ns CW and 250-750 keV EW can yield a good NECR for the typical range of radioactivity used in FDG-PET imaging with mice, yielding a peak NECR value of ~1.86 Mcps at a total activity of ~32 MBq. On the other hand, the NECR curve obtained by use of the 6 ns CW and 350-750 keV EW, yielding a peak value of ~1.2 Mcps at a total activity of ~40 MBq, is appropriate for the typical range of radioactivity used in FDG-PET imaging with rats. Figure 6 shows the NECR curves of the prototype when using a 10 ns CW and various EWs, along with the peak locations of the NECR curves reported in the literature for other μPET systems [3,19]–[21,40]–[55]. Also shown are the maximum-slope lines of these peaks. Since the rising portion of a NECR curve can be approximated by a straight line, these maximum-slope lines estimate the maximum NECRs of other μPET systems been examined. It shall be noted that the reported NECRs are obtained by using various phantom sizes; therefore, caution must be exercised when making comparisons. It is however evident that the NECR of our prototype is significantly higher than the NECRs of other existing μPET systems over the typical ranges of radioactivity used for performing FDG-PET imaging of rodents.

Figure 7 compares the NECR curves obtained by measurement and by MC simulations with the system dead-time ignored. It is observed that the simulated and measured results agree reasonably well with each other when the dead-time effect is negligible. Also, the dead-time effect of our prototype is not small. The peak values of the simulated NECR curves are about twice the measured values. Also, the activities where peaks occur are about three times the activities where the peaks of the measured NECR curves occur. Therefore, the count-rate performance of our prototype is far from what its hardware configuration can potentially achieve. This is not surprising given that the HRRT detector technology is not...
Our prototype is much more sensitive and hence much lower radioactivity can be used, further alleviating the concern for the limited count-rate performance of the prototype.

Generally speaking, if the CWs and EWs reported in the literature for other existing μPET systems are used in rodent imaging. It needs to be noted that these “typical” ranges are determined for existing μPET systems. The dashed lines are the maximum-slope lines of these reported NECR peaks. These lines provide estimates of the maximum NECRs available with other existing μPET systems. The vertical bars show the typical ranges of radioactivity employed in current FDG-PET imaging of mice and rats.

net sensitivity of a PET scanner with the negative impact of the scatter events taken into account. Figure 8 shows the NES obtained for our prototype. It indicates that a net sensitivity as high as 28.3% and 23.2% can be achieved for the mouse- and rat-sized subjects, respectively.

C. DOI blurs

As already mentioned above, due to its compact geometry our prototype exhibits substantial DOI blurs. To demonstrate, Fig. 9 shows the sensitivity functions of 7×5 LORs to points on the midplane between the two detectors of the prototype, obtained by using MC simulations. The long axes of these sensitivity functions reflect the directions of the LORs projected onto the midplane. It is evident that the sensitivity function grows wider for more oblique LORs. Specifically, the sensitivity function of the vertical LOR is isotropic and has a FWHM of 1.2 mm. In comparison, the sensitivity function of

Figure 5. NECR curves for the mouse- and rat-sized cylinders when using various CWs and EWs. The results are derived from the count-rate measurements shown in Fig. 4 and the vertical bars indicate the typical ranges of radioactivity used in FDG-PET imaging of mice and rats.

Figure 6. Comparison of the NECR curves of the prototype, obtained by use of a 10 ns CW and various EWs, with the NECR peaks (black squares) reported in the literature for other existing μPET systems. The dashed lines are the maximum-slope lines of these reported NECR peaks. These lines provide estimates of the maximum NECRs available with other existing μPET systems. The vertical bars show the typical ranges of radioactivity employed in current FDG-PET imaging of mice and rats.

Figure 7. Measured and simulated NECR curves for the mouse- and rat-sized cylinders for CW=6 ns and EW=350-750 keV. Scatter fractions estimated by MC simulation were used for calculating the measured NECR curves. In MC simulation, 20% energy resolution and 3 ns coincidence timing resolution are assumed.
functions demonstrate that substantial DOI blurs are present with the \( \mu \)a 1.4 mm FWHM and its long axis has a 8.0 mm FWHM. These sensitivity with the most oblique LOR of the 35 LORs been examined. Its short axis has has an FWHM of 1.2 mm. The lower-right sensitivity function is associated associated with an LOR that is vertical to the detector heads. It is isotropic and isotropic of the LORs projected onto the midplane. The upper-left sensitivity function is function of the prototype due to its compact geometry.

Figure 8. The noise-equivalent sensitivity (NES) obtained for our prototype. Symbols show the measured NECR curves obtained with various LLD settings for the EW (the ULD equals 750 keV) and the solid lines are their tangents. The slopes of these tangents, i.e., the NES values, are indicated. An NES of \(-28.3\%\) \((-23.2\%)\) can be obtained for the mouse-sized (rat-sized) cylinder when using a 200-750 keV EW and 10 ns CW.

Figure 9. Images showing the sensitivity functions of 7 \( \times \) 5 LORs of the prototype to points on the midplane between the two detectors of the prototype. The long axes of these sensitivity functions reflect the directions of the LORs projected onto the midplane. The upper-left sensitivity function is associated with an LOR that is vertical to the detector heads. It is isotropic and has an FWHM of 1.2 mm. The lower-right sensitivity function is associated with the most oblique LOR of the 35 LORs been examined. Its short axis has a 1.4 mm FWHM and its long axis has a 8.0 mm FWHM. These sensitivity functions demonstrate that substantial DOI blurs are present with the \( \mu \)PET prototype due to its compact geometry.

the most oblique LOR shown has a 1.4 mm FWHM along its short axis and a 8.0 mm FWHM along its long axis.

We have performed some initial measurements to validate the spatial response functions generated by MC simulations. We employed a spinal needle, having an external diameter of 0.74 mm; filled it with FDG; and placed it parallel to the detectors of the prototype. We obtained reconstructed images of the spinal needle without correcting for the DOI blurs and extracted the axis of the needle from the resulting images. Then, fan-beam projection images of the needle were calculated by using the location of the derived axis and the response functions that are calculated either by using MC simulations (which models the DOI blurs) or by using a ray-tracing technique (which assumes the ideal line-integral projection model). The finite diameter of the spinal needle was not considered in these computations. Figure 10 compares several measured profiles of the fan-beam projection images of the spinal needle with the calculated profiles. The results indicate that the calculated profiles obtained by using the MC-generated response functions agree reasonably well with the measured ones. On the other hand, the calculated profiles obtained by using the raytracing-generated response functions show substantial differences with the measured profiles.

D. Resolution phantom

The image resolution of the scanner was evaluating by a resolution phantom (Ultra-Micro Hot Spot phantom, Data Spectrum Corporation) that consists of rod sources of various diameters, ranging from 0.75 mm to 2.4 mm. The phantom was filled with ~70\( \mu \)Ci of FDG, placed with its axis vertical to the detectors, and scanned for two hours. The data were corrected for randoms (by subtracting the delayed events) and normalized, but no scatter and attenuation corrections were performed. Reconstruction was achieved by using an OSEM algorithm that employed with the MC- or raytracing-generated response functions. Figure 11 shows the resulting images obtained from the same data. Evidently, when employing the MC-generated response functions the 1.35 mm rods are clearly visible and there is a hint for the 1.0 mm rods. This result is consistent with the 1.2 mm image resolution that we previously obtained with simulated data [38,39]. In contrast, the image obtained by using the raytracing-generated response functions contains significant blocky artifacts. We suspect that these artifacts are due to the amplifications of the modeling errors by the reconstruction process.

E. Real-data rat images

We have also employed our high-sensitivity prototype for imaging rodents. Figure 12 shows the maximum-intensity projection (MIP) images obtained at two view angles for a 270g healthy rat, from a 20-minute dataset acquired at 40 minutes post-injection of \(~700\mu \)Ci of FDG. The energy and coincidence windows were 350-650 keV and 6 ns, respectively. Randoms correction was achieved by subtracting the delayed events from the prompt events. Again, no corrections for scatter and subject attenuation were applied. The DOI blurs associated with the prototype were corrected for by use of the reconstruction method described in [39,56]. Figure 13 similarly shows the results obtained from a 1-minute dataset obtained at 30 minutes post injection. These results demonstrate that reconstruction with the real data is successful. No significant image artifacts are observed even though data produced by the scanner are in theory incomplete (see discussion in Sect. II.B).

IV. Conclusions and Discussion

We have developed a high-sensitivity \( \mu \)PET prototype that can reach a central sensitivity of \(~30\%)\ and an image resolution of \(~1.2\) mm. Over the typical ranges of radioactivity currently used for conducting FDG-PET rodent imaging, the NECR and
Figure 10. Sample intensity profiles of the measured projection images of a spinal needle, filled with FDG, in comparison with the predicted profiles obtained by using spatial response functions calculated for the prototype. The spatial response functions are computed either by using MC simulations that include the DOI blurs of the scanner, or by using a ray-tracing technique that assumes the ideal line-integral projection model. We note that the MC-predicted response functions agree reasonably well with the measurements. Note that the spinal needle has an external diameter of ~0.74 mm.

Figure 11. Cross-sectional images of a resolution phantom (Ultra-Micro Hot Spot phantom, Data Spectrum Corporation) obtained by using two iterations of an OSEM algorithm that employs MC- (left) and raytracing-generated (right) response functions. The phantom contains six groups of rods having diameters of 2.4 mm, 2.0 mm, 1.70 mm, 1.35 mm, 1.0 mm and 0.75 mm. The spacing between two neighboring rods in the same group is twice their diameter. The data were corrected for randoms, but not for attenuation and scatter. The 1.35 mm rods are clearly visible in the MC image.

NES of the prototype are significantly higher than the those of other $\mu$PET systems reported in the literature. A significant component of the scanner design is the application of a new synergistic design concept. By adopting this design concept, we are able to employ an off-the-shelf detector technology – the HRRT technology – for reaching the high performance targets that would otherwise have to wait after more advanced detector technologies to become available. It is important to note that the design of the HRRT detector is cost effective with respect the detection performance it provides, and to emphasize that, without the use of the synergistic design concept, the performance properties of the HRRT detectors are insufficient for meeting the desired performance targets (see Sect. II.B). Because the HRRT detectors are not designed for use in high-sensitivity applications of concern in this paper, the count-rate capability of the prototype is somewhat limited. However, our results indicate that it is still adequate for handling the typical ranges of radioactivity used in FDG-PET imaging of rodents.

The results obtained with our prototype have validated the application of the new synergistic design concept for overcoming the performance limitations of given detector technologies, thereby enabling cost-effective development of high-performance PET systems. This design concept is general and can be applied to any detector technologies. Currently, little systematic information is available to guide this synergistic design concept. The development presented in this paper is based largely on qualitative observations (see Sects. II.A and II.B) and our experience with model-based image reconstructions. We plan to conduct a series of theoretical investigations to generate systematic knowledge in order to turn this useful concept into more solid design principles. For this purpose, the theoretical frameworks developed by Qi et al. [57,58] and Fessler et al. [59] are valuable.

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REFERENCES

Figure 12. MIPS images of a 270g healthy rat, at two different views, generated from a 20-minute dataset acquired at 40 minutes after a bolus injection of ~700 µCi FDG. Randoms are corrected for by subtracting the delayed events. Scatter and subject attenuation are not corrected for.


Figure 13. MIPS images of a 270g healthy rat, at two different views, generated from a 1-minute dataset acquired at 30 minutes after a bolus injection of ~700 µCi FDG. Randoms are corrected for by subtracting the delayed events. Scatter and subject attenuation are not corrected for.


