Published in final edited form as:

IEEE Trans Nucl Sci. 2016 February ; 63(1): 75–83. doi:10.1109/TNS.2015.2482459.

TandemPET- A High Resolution, Small Animal, Virtual Pinhole-Based PET Scanner: Initial Design Study

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Abstract

Mice are the perhaps the most common species of rodents used in biomedical research, but many of the current generation of small animal PET scanners are non-optimal for imaging these small rodents due to their relatively low resolution. Consequently, a number of researchers have investigated the development of high-resolution scanners to address this need. In this investigation, the design of a novel, high-resolution system based on the dual-detector, virtual-pinhole PET concept was explored via Monte Carlo simulations. Specifically, this system, called TandemPET, consists of a $5\text{ cm} \times 5\text{ cm}$ high-resolution detector made-up of a 90×90 array of $0.5\text{ mm} \times 0.5\text{ mm} \times 10\text{ mm}$ (pitch= 0.55 mm) LYSO detector elements in coincidence with a lower resolution detector consisting of a 68×68 array of $1.5\text{ mm} \times 1.5\text{ mm} \times 10\text{ mm}$ LYSO detector elements (total size= $10.5\text{ cm} \times 10.5\text{ cm}$). Analyses indicated that TandemPET's optimal geometry is to position the high-resolution detector 3 cm from the center-of-rotation, with the lower resolution detector positioned 9 cm from center. Measurements using modified NEMA NU4-2008-based protocols revealed that the spatial resolution of the system is $\sim 0.5\text{ mm}$ FWHM, after correction of positron range effects. Peak sensitivity is 2.1%, which is comparable to current small animal PET scanners. Images from a digital mouse brain phantom demonstrated the potential of the system for identifying important neurological structures.

Index Terms

Monte Carlo Simulation; PET Instrumentation; Small Animal Imaging

I. INTRODUCTION

The size, hardy nature and rapid reproduction rates of rodents, mainly rats and mice, make them ideal for use in biomedical research. While there have been a large number of disease

models developed for both species, mouse models have become predominant. There are almost twice as many mouse disease models as rat models available from commercial vendors. This prevalence is due to the mouse's close genetic and physiological similarities to humans, and the ease with which its genome can be manipulated and analyzed.

Prior to introduction of high resolution imaging techniques in the 1990s, animal research often required dissection to examine various aspects of a disease model's progression and/or its effect on physiology and anatomy. With development of high resolution PET [1–2], SPECT [3–4], CT [5–6] and MRI [7–8] scanners, designed specifically for imaging of small animals, the necessity for dissection was reduced, enabling longitudinal studies on a relatively small cohort of animals. Of particular interest to many researchers, is the application of metabolic imaging techniques with radiopharmaceuticals targeted to physiological processes.

Beginning with the MicroPET[®] series of scanners [1], the spatial resolution of preclinical PET systems has progressively improved. Scanners with resolutions from 1.6 mm to 2.3 mm FWHM [9] are now available, making them most appropriate for imaging of rats, due to the large size of their anatomy relative to scanner resolution. These systems are less effective for the imaging of small structures in mice, some of which have linear dimensions less than 1 mm [10]. Higher resolution PET scanners designed for mouse imaging are necessary not only to permit identification of small anatomical features, but also to accurately quantify the amount of radiotracer present in these structures by effectively compensating for the partial volume effect. Consequently, some researchers have investigated construction of scanners with sub-millimeter resolution [11–18].

Rodriguez-Villafuerte, *et al.* have investigated, via Monte-Carlo simulations, a mouse-PET scanner based on a ring of sixteen detector modules (14×14 arrays of tapered LSO elements ($0.45 \text{ mm} \times 0.45 \text{ mm}$ at the entrance end increasing to $0.45 \text{ mm} \times 0.814 \text{ mm}$ at the exit end)). The modules use PSAPDs to read out both ends of the array to allow measurement of photon depth-of-interaction (DOI) in the scintillator [19]. They reported spatial resolution of $\sim 0.66 \text{ mm}$ FWHM at the center of the simulated scanner, increasing to $\sim 0.77 \text{ mm}$ FWHM, 8 mm from its center (assuming a DOI resolution of 2 mm). While this scanner, like most scanners, employ the conventional ring detector geometry, this design presents some potential weaknesses when applied to high-resolution PET imaging. For example, the relatively large number of scintillator arrays consisting of very small detector elements necessary to populate the rings of these scanner are labor intensive to construct and expensive. Additionally, DOI-capable detector modules (required for high resolution PET scanners) detect light from both ends of the scintillator arrays, increasing their cost. Finally, formation of a ring scanner from flat detector modules result in reduced photon detection sensitivity at the interfaces where the modules meet. These areas cause gaps in sinograms, potentially producing artifacts in the reconstructed images. Consequently, specialized methods have to be applied to correct for these gaps in data [19–25].

In addition to the conventional ring scanner geometry, the virtual-pinhole PET concept (developed by Tai, *et al.* [26]) has been proposed for the creation of high-resolution scanners [27–30]. In the most common application of this technique, a high-resolution detector,

utilizing small cross section scintillator elements, is connected in coincidence with a lower resolution PET scanner, resulting in a system with resolution close to the physical size of the high-resolution detector's scintillator elements.

A virtual-pinhole PET scanner's spatial resolution is determined by the size of the scintillator elements and the relative positions of the detectors. The relationship between element sizes and distances, and spatial resolution at the center-of-rotation (COR) is given by [26]:

$$R_{\text{sys}} \approx \sqrt{R_{\text{src}}^2 + \left[0.0088 \cdot \frac{d_1 \cdot d_2}{(d_1 + d_2)} \right]^2 + \left[\frac{d_2 \cdot w_1 + d_1 \cdot w_2 + |d_2 \cdot w_1 - d_1 \cdot w_2|}{2 \cdot (d_1 + d_2)} \right]^2}. \quad (1)$$

Where, R_{src} is the effective source size (assuming zero positron range), d_1 is the distance from the high-resolution detector to the COR, d_2 is the distance from the lower resolution detector to the COR, w_1 is the width of the high-resolution detector elements and w_2 is the width of the lower resolution detector elements.

Wu *et al.* constructed a virtual-pinhole scanner insert designed to be placed in the bore of a Siemens MicroPET[®] F-220 [27]. The high resolution insert consisted of a ring of eighteen modules each constructed from a 12×12 array of $0.72 \text{ mm} \times 1.51 \text{ mm} \times 3.75 \text{ mm}$ LSO elements, separated by reflective film (pitch = $0.8 \text{ mm} \times 1.59 \text{ mm}$). The insert outputs were integrated into the MicroPET[®]'s coincidence processing electronics. Performance testing showed that in the central 2 cm of the field-of-view (FOV), the tangential spatial resolution of the scanner is $\sim 0.9 \text{ mm}$ FWHM and the radial resolution is $\sim 0.6 \text{ mm}$ FWHM. The theoretical resolution limit for this scanner geometry measured with ^{18}F is $\sim 0.7 \text{ mm}$ [31–32]. This limitation is due to the effects of positron range and photon acolinearity. Note that the maximum positron energy of ^{22}Na positrons is 545 KeV compared to 635 KeV for ^{18}F , so the resolution limit for ^{22}Na is expected to be slightly lower than that reported for ^{18}F . The peak detection sensitivity of the scanner is 2.7%, which is 11% lower than the peak sensitivity of a MicroPET[®] F-220 [27]. Some of this loss of sensitivity is due to the use of only three of the four detector rings in the F-220 to permit integration of the insert. There is also some absorption of photons in the support structure of the insert in the FOV of the MicroPET[®], thus reducing the detection sensitivity of the system.

To create a very high-resolution PET scanner suitable for the imaging of mice, we studied a system based on the dual-detector variant of a virtual-pinhole scanner. This system, called TandemPET, consists of a pair of rotating detectors. The goal of this investigation is to explore TandemPET's design and predict its imaging performance via calculations and Monte Carlo simulations.

II. METHODS

A. TandemPET Geometry Study

TandemPET consists of one small, high-resolution detector and one larger, lower resolution detector. Specifically, the high-resolution detector utilized a 90×90 array of $0.5 \text{ mm} \times 0.5 \text{ mm} \times 10 \text{ mm}$ (pitch = 0.55 mm) LYSO detector elements (total detector size = $5 \text{ cm} \times 5 \text{ cm}$).

This size of LYSO element is the smallest that can be reliably formed into a stable array without the necessity of a costly and bulky external structure. Since this detector was located close to the COR and the detector elements are narrow, the localization of events in the scintillator array was subject to DOI effects. Therefore, this detector requires the ability to measure the depth of each event in the detector elements. This task was accomplished by using dual ended readout of the scintillator array, with a DOI detection resolution of 2 mm [33]. The lower resolution detector consisted of a 68×68 array of $1.5 \text{ mm} \times 1.5 \text{ mm} \times 10 \text{ mm}$ (pitch= 1.55 mm) LYSO detector elements (total size= $10.5 \text{ cm} \times 10.5 \text{ cm}$). Choice of detector element size was based on ease of construction and cost. Due to increased distance from the COR and wider elements, this detector does not require measurement of event depth in the scintillator.

To study TandemPET's optimal geometry, spatial resolution as a function of total detector separation and distance from the high-resolution detector to the COR was calculated with Eq. 1 ($R_{\text{src}} = 0.0125 \text{ mm}$) and plotted. The results (shown in Fig. 1) indicate that highest resolution (0.4 mm to 0.5 mm FWHM) was achieved with a total detector separation of between 80 mm and 160 mm, and a distance of between 20 mm and 40 mm from the COR to the high-resolution detector. As a compromise between spatial resolution and detection sensitivity (gauged by detector separation), it was decided to design TandemPET with a geometry having dimensions that fell within the central region of the optimal range (total separation= 120 mm; high-resolution detector distance to COR= 30 mm). This geometry also permits sufficient space to include a front-side readout of the scintillator array to facilitate measurement of DOI. Fig. 2 shows drawings of the TandemPET scanner.

One of the motivations for using the dual detector, virtual pinhole scanner design versus other designs was overall cost of the system. Specifically, TandemPET's design limits the total amount of scintillator elements, light detection devices and data acquisition channels required to build the system. Reducing the amount of these small elements reduces the cost and complexity of TandemPET compared to a scanner made-up of a pair of rotating high-resolution detectors or one consisting of a ring of these detectors. Another motivation for utilizing the dual detector, virtual pinhole PET scanner is the flexibility to adjust its geometry to produce a system with a desired spatial resolution and detection sensitivity (determined by detector separation) as demonstrated in Fig. 1.

B. Scanner Simulations

1) Measurement of Spatial Resolution—Once the scanner's geometry was identified, its potential imaging capabilities were explored by performing a series of computer simulations using the GATE software package operating on a thirty two-core computer cluster [34]. The tests were based on the NEMA NU4-2008 protocols [35]. First, a simulated 0.025 mm-diameter ^{18}F (50 μCi) point-like source embedded in an acrylic cube (1 cm^3) was stepped along the x-axis at $z = 0 \text{ cm}$ ($x = -1.5 \text{ cm}$ to 1.5 cm , in steps of 5 mm). Data were acquired for 90 s (18 steps of 20° , 5 s/step). Unless specifically noted, the presence of positron range, Compton scattering, photon attenuation, detector dead time and random coincidences were modeled in all simulations. Inclusion of positron range and photon acolinearity in the simulations was particularly relevant for this study since their presence

has the potential for degradation of high resolution PET images [31–32]. To determine the effects of these two phenomena on spatial resolution, simulations were performed for the four possible combinations of positron range present and not present, and photon acolinearity present and not present.

The NEMA NU4-2008 protocol for measuring spatial resolution requires the use of filtered backprojection reconstruction. Due to TandemPET's unique geometry this method could not be used. Instead, data were reconstructed using an ordered subset expectation maximization (OSEM) algorithm (12 iterations and 3 subsets). The FWHM of the image of the point source stabilized at 12 iterations. Image reconstructions were performed with DOI correction of the data from the high-resolution detector (the 10 mm-thick scintillator crystal was divided into five, 2 mm-thick layers). Detector response was modeled as a one-voxel FWHM Gaussian function. A ray tracing method using a 3D adaptation of Siddon's algorithm was used to obtain the system matrix. Endpoints of lines of response were randomized within boundaries of the detector elements to minimize system bias [36]. Photon attenuation was corrected using calculations from the known size and shape of the phantoms. The reconstructed FOV had a diameter of 1.8 cm and an axial extent of 2.5 cm. The image voxel size was 0.25 mm × 0.25 mm × 0.25 mm.

2) Correction for the Effects of Positron Range—For most PET scanners, the effect of positron range does not affect spatial resolution by any appreciable amount due to the fact that their resolutions are much larger than the range of positrons emitted by most PET radionuclides. Based on the calculations shown above, TandemPET's spatial resolution was expected to be ~0.45 mm FWHM. Thus, the range of positrons, even those emitted by ^{18}F , which have a mean and maximum range of ~0.6 mm and ~2.4 mm, respectively [31–32], will degrade the system's resolution. To correct images for this effect, a modified version of the deconvolution method described by Derenzo [37] was developed. Specifically, the image data was deconvolved with a kernel based on the positron range distribution for ^{18}F , which is given by a biexponential function [31–32]:

$$R(x) = Ce^{-k_1|r|} + (1 - C)e^{-k_2|r|}. \quad (2)$$

For ^{18}F , $C = 0.516$, $k_1 = 37.9 \text{ mm}^{-1}$ and $k_2 = 3.1 \text{ mm}^{-1}$. The value r is the radial distance from the positron emission:

$$r = \sqrt{x^2 + y^2 + z^2}. \quad (3)$$

Where, x , y and z are the spatial dimensions in image space. The Fourier transform of the positron range distribution function ($R(\omega)$) is given by:

$$R(\omega) = \frac{2Ck_1}{k_1^2 + \omega^2} + \frac{2k_2(1 - C)}{k_2^2 + \omega^2}. \quad (4)$$

The symbol ω represents the spatial frequency in image space. If the image data were deconvolved with $R(\omega)$, noise in the data would be amplified. To reduce this effect, it was

necessary to modify $R(\omega)$ by combining it with a function that filters higher frequencies ($H(\omega)$) given by:

$$H(\omega) = 1 + \left(\left(\frac{\omega}{\omega_c} \right)^2 \times (R(\omega) - 1) \right). \quad (5)$$

The symbol ω_c represents the cutoff frequency and n is the order of the polynomial defined by the frequency-to-cutoff frequency ratio (higher orders enhance high frequencies). The deconvolution kernel ($G(\omega)$) is given by:

$$G(\omega) = \frac{R(\omega)}{H(\omega)} = \frac{R(\omega)}{1 + \left(\left(\frac{\omega}{\omega_c} \right)^n \times (R(\omega) - 1) \right)}. \quad (6)$$

If $|\omega| \leq \omega_c$, $G(\omega) = 1$. Deconvolution of the image data was accomplished by dividing the Fourier transform of the image data by $G(\omega)$ and then transforming back into image space. The values for ω_c (1.5/mm (Nyquist frequency = 2/mm)) and n (4) used in this study were empirically determined to maximize spatial resolution and minimize noise amplification.

3) Measurement of Detection Sensitivity—Detection sensitivity was measured by stepping a ^{22}Na point source along the axis of rotation of the scanner (z-axis) in increments of 1 cm. At each source position, data were acquired for 90 s (18 steps of 20° , 5 s/step). The total number of detected events in the energy window (350 keV to 650 keV) were measured and used to calculate slice and system sensitivity.

4) Simulated Imaging of a Modified NEMA NU4-2008 Image Quality Phantom—

To measure image uniformity, recovery coefficient and spillover, a modified NEMA NU4-2008 Image Quality Phantom was simulated. The dimensions of the standard phantom were reduced by a factor of two to make it more appropriate to assess the performance of TandemPET. Specifically, the inner diameter of the new phantom was 15 mm, the uniform section of the phantom was 10 mm long, the spillover ratio measurements section contained two (one filled air and the other with water) 7.5 mm long cylinders with diameters of 5 mm in a uniform background, the recovery coefficient measurement section contained five, 7.5 mm long cylinders (diameters = 0.5 mm, 1 mm, 1.5 mm, 2.0 mm and 2.5 mm). The phantom contained 200 μCi of ^{18}F ; it was scanned for 90 s (18 steps of 20° , 5 s/step).

5) Simulated Imaging of a micro-Hot Rod Phantom—A Derenzo-like, micro-hot rod phantom was simulated to illustrate the high resolution imaging capabilities of TandemPET. This phantom consisted of four, 4×4 arrays of rods filled with water containing ^{18}F . The diameters of the rods are: 1.0 mm, 0.8 mm, 0.6 mm and 0.5 mm. Rod pitch was twice the diameter of each rod. The phantom contained a total of 100 μCi of ^{18}F ; it was scanned for 90 s (18 steps of 20° , 5 s/step).

6) Simulated Imaging of a Mouse Brain—Finally, to demonstrate the potential improvement of mouse imaging achievable with TandemPET, the brain section of the 4D Mouse Whole Body (MOBY) digital phantom (v2.0) [38] was scanned for 90 s (18 steps of 20° , 5 s/step). The same phantom was also scanned with a simulated Siemens MicroPET[®]

Focus 120 scanner [39]. The amount of activity in each of the brain's structures was adjusted to simulate a 200 μCi injection of ^{18}F -Fluorodeoxyglucose (FDG) [40].

III. RESULTS

The two plots in Fig. 3 show spatial resolution as a function of source position. In each plot, the results for simulations that did and did not include positron range are shown. The results obtained from images that were corrected for the effects of positron range are also shown. To assess the effect of photon acolinearity, measurements were made without (Fig. 3(a)) and with (Fig. 3(b)) the effects of photon acolinearity included in the simulations. The plot of detection sensitivity as a function of source position along the axis of rotation is shown in Fig. 4. The peak slice sensitivity is 2.1% at the center of the scanner. The total system sensitivity is 6.2%.

Fig. 5 shows a coronal image of the digital microNEMA-NU4 Image Quality Phantom described above. The percent standard deviation of the mean counts measured in the uniform section of the phantom was 1.7% without application of positron range correction and 3.0% with application of positron range correction. The increase in standard deviation following correction of positron range effects is due to some noise amplification produced by our method. Images of the micro-rod section of the phantom were used to calculate the recovery coefficient for each rod. Fig. 6 shows a plot of recovery coefficient as a function of rod diameter (with and without positron range correction). Images of the dual cylinder section of the phantom (one filled with air, one with water) were used to assess the effect of Compton scatter on the images. The spillover ratio for the positron-range corrected images for the air-filled cylinder was $10.0 \pm 1.2\%$ and $36.0 \pm 5.5\%$ for the water-filled cylinder. For the uncorrected images, the spillover ratio for images of the air-filled cylinder is $21.2.0 \pm 1.8\%$ and $35.1 \pm 3.1\%$ for the water-filled cylinder. The uncorrected effect of positron penetration (and their resulting annihilation) into the air-filled cylinder was the cause for the higher spillover of counts in the uncorrected images compared to the corrected. In the water-filled cylinder, the positrons do not penetrate as far into the cylinder. Thus, positron range correction does not have as great of an effect for this region compared to the higher-density, water-filled region; most of the spillover is hence due to the presence of Compton-scattered photons.

Fig. 7 shows an image of the micro-hot rod phantom, without (a) and with (b) the correction for positron range applied. The peak-to-valley ratios (PVR) measured for the four areas of rods of the images shown in Fig. 7 are given in Table I. Fig. 8 shows slices from images of the brain section of the MOBY phantom; the effect of positron range and its correction are illustrated. Specifically, the application of the correction enhances separation of images of the caudoputamen and amygdala from the hypothalamus and thalamus. Note that the size, shape and orientation of the image of the amygdala shown in Fig. 8(d) match well with their size, shape and orientation shown in the image of the phantom (Fig. 8(a)).

IV. DISCUSSION

The development and continuing advancement of PET scanners designed for small animal imaging since the 1990s has demonstrated the value of these devices to medical and

pharmaceutical research. While the brains of mice have been imaged with some of these scanners, the small size of many of the anatomical structures in this organ compared to the resolution of current systems limit the scope of these studies. In this work we investigated a novel method for constructing a high-resolution PET scanner, while limiting overall cost by designing a system based on the dual detector variant of the virtual-pinhole concept.

A series of Monte Carlo simulations were performed to assess the spatial resolution and other performance characteristics of the scanner. The results shown in Fig. 3 demonstrate that the resolution measured for TandemPET from images that did not include effects from positron range (~ 0.43 mm FWHM) compare relatively well with the resolution calculated with Eq. 1 (~ 0.45 mm FWHM). Furthermore, the resolution measured from images that included positron range effects (~ 0.6 mm FWHM) agree relatively well with theoretical limit of PET scanner resolution calculated by Levin and Hoffman for a scanner with TandemPET's detector size and diameter [31]. To reduce the effect of positron range on scanner resolution, TandemPET images were deconvolved with a kernel derived from the positron range distribution function for ^{18}F . Correction of the range effects improved resolution from ~ 0.6 mm FWHM to ~ 0.5 mm FWHM. These results are better than the 0.66 mm FWHM predicted for the proposed mouse scanner described by Rodriguez-Villafuerte, *et al.* [19] and the resolution measured by Wu, *et al.* (0.6 mm FWHM) for their modified MicroPET[®] F-220 scanner [27]. The correction process did not completely recover the ~ 0.43 mm FWHM measured for the source without positron range and photon acolinearity partly because the choices for the order of the polynomial and cutoff frequency used for the filter function $H(\omega)$ were a compromise between resolution recovery and noise amplification. A more robust solution to empirical adjustment of the filter parameters is to incorporate positron range effects in the scanner model used in the reconstruction algorithm. An effort to include positron range effects in the reconstruction algorithm is underway.

To put the resolution results in context: Larobina, *et al.* estimated that to image a mouse brain at the equivalent resolution of a human brain scanned by a clinical PET scanner with a resolution of 5 mm FWHM, a mouse scanner has to have a resolution of ~ 0.4 mm FWHM [41]. Thus, the predicted resolution of TandemPET approaches the equivalent of a high-resolution human brain imager. While these results are promising for the improved PET imaging of the mouse brain, it should be noted that the number of gyri in the mouse brain is much lower than in the human brain and features in the cortex are challenging to visualize, even with high spatial resolution MRI scanners.

The results in Fig. 3 also demonstrate that there was little dependence of resolution on source position. This behavior was consistent with the use of DOI correction. Additionally, the similarity of the results in Fig. 3(a) (measured from images created without inclusion of the effect of photon acolinearity) and Fig. 3(b) (measured from images that included the effect of photon acolinearity) indicate that TandemPET's geometry is resistant to degradation caused by acolinearity of annihilation photons. Specifically, the small overall separation of the detectors (12 cm) and particularly the small distance between the COR and the high-resolution detector (3 cm) minimizes the physical length over which the small photon angular dispersion from 180° produces an offset in event positioning.

The results shown in Fig. 4 demonstrate that the shape of the detection sensitivity profile of TandemPET is similar to most conventional PET scanners. Likewise, the peak sensitivity (2.1%) compares well with conventional small animal PET scanners [9] and with the 2.7% peak sensitivity reported by Wu, *et al.*, for their small animal insert using the virtual-pinhole PET concept [27]. It is somewhat surprising that the sensitivity of TandemPET is comparable to ring geometry scanners given the seemingly sparse solid angle coverage of the twin detector geometry, but the size of the detectors and their close proximity to the COR offset the coverage advantage of ring-detector based scanners. The detection sensitivity of future versions of TandemPET could be doubled by adding a second set of detectors, with the penalty of increasing system cost.

To accommodate the high resolution of TandemPET and challenge its performance, a digital microNEMA-NU4 Image Quality Phantom was created. Images, such as the one shown in Fig. 5, were used to perform the measurements described in the NEMA NU4-2008 protocol [35]. Results from the measurement of image uniformity demonstrate that application of the positron range correction introduces minimal non-uniformities. This finding, in addition to the results shown in Fig. 3, verifies the effectiveness of the compromises made in the deconvolution filter parameters discussed above (good resolution with relatively small noise amplification).

The plot of recovery coefficients from the positron range-corrected images versus rod diameter (Fig. 6) demonstrates that the high spatial resolution of TandemPET could aid in making more accurate measurements of radiotracer concentration in mouse structures than is possible with current scanners. For example, ~40% of the signal from the 1 mm-diameter rods was recovered; this value is almost a factor of two higher than the highest recovered signal from the 1 mm-diameter rod reported for conventional small animal PET scanners (27% for the Sedecal Argus system) [9]. The higher recovery coefficients for the positron range-corrected images compared to the uncorrected images are due to the improved spatial resolution (illustrated in Figure 3) resulting from application of the correction.

Spillover ratios measured for the positron range-corrected images of the air- and water-filled cylinders are relatively high ($10.0 \pm 1.2\%$ and $36.0 \pm 5.5\%$, respectively). Values for the water-filled cylinder ranging from ~9% to ~37% have been reported for some of the currently available small animal PET scanners [9]. Our results are in the upper part of this range because of the current lack of a method to correct the images for the presence of Compton-scattered photons. We are currently working to incorporate correction for Compton scattering into the image reconstruction process.

Images of the micro-hot rod phantom shown in Fig. 7 illustrate TandemPET's high-resolution capabilities. These images also demonstrate the necessity for application of the positron range correction to take full advantage of the high-resolution capabilities of TandemPET. This conclusion is supported by results for measurements of PVR (Table I). Specifically, measurements for all of the rods have higher contrast (as gauged by PVR) following correction for the corrected versus uncorrected data. Note, that the 0.5 mm-diameter rods are not well defined in either image, illustrating the resolution limit of the system.

Finally, TandemPET's performance and the effect of positron range on the imaging of the mouse brain were assessed by scanning a digital phantom (Fig. 8). Comparison of Fig. 8(b) (image acquired with a simulated MicroPET[®] Focus 120) with the phantom (Fig. 8(a)) illustrate the limitations of PET scanners with millimeter scale resolution in FDG imaging of the mouse brain. Some of the larger regions of the brain can be identified, whereas definition of smaller regions are lacking. Fig. 8(c) shows that higher resolution imaging (sub-millimeter resolution) with TandemPET provides slightly better localization of FDG in the areas of the brain, but it is still difficult to identify the smallest structures (amygdala and caudoputamen). These structures are not discernable until the TandemPET images are corrected for positron range (Fig. 8(d)).

V. CONCLUSIONS

In summary, a new type of scanner utilizing the dual detector variant of the virtual-pinhole PET concept was evaluated, through Monte Carlo simulations, for use in the scanning of mouse brains. This device, known as TandemPET, was shown to possess very good imaging capabilities (high spatial resolution, good detection sensitivity and good image uniformity). High spatial resolution and detection sensitivity are important to obtain accurate measurements of radiopharmaceutical concentrations in very small structures in the brains of mice.

While there are potential advantages of high-resolution PET imaging with TandemPET, there are also potentially some challenges. Specifically, degradation of spatial resolution caused by photon acolinearity and positron range, normally of minor consequence to most PET scanners, must be addressed in high-resolution (sub-millimeter resolution) scanners. The effects of these processes were reduced by careful design of TandemPET's geometry and application of correction schemes.

Perhaps the most notable deficiency of the current design of TandemPET is the lack of the ability to rapidly acquire data, limiting the temporal resolution of the system. Thus, it is challenging to acquire information concerning the kinetics of radiopharmaceuticals. This weakness could be mitigated by the addition of a second set of detectors, effectively doubling the temporal resolution of the system. Continually rotating the detectors, instead of stepwise motion, could also improve temporal resolution. Another potential limitation for acquiring quantitative data with TandemPET is the current lack of a method for correction of photon attenuation in animals. This deficiency can be addressed by the incorporation of a CT scanner into the TandemPET gantry. Finally, this study is limited by the fact that all of the results were obtained via calculation or simulation. No matter how well considered the calculation or accurate the simulation, they cannot replace measurements from a real system. Thus, the next step in the project is construction of a prototype system.

Acknowledgments

This work was supported in part by the National Institutes of Health R01 CA094196 and R01 EB007349.

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Fig.1.
Surface plot of spatial resolution as a function of detector separation and distance from the COR.

Fig. 2. Conceptual drawings of the TandemPET scanner. (a) End view showing the scanner gantry and (b) top view showing dimensions of the scanner.

Fig. 3.

Plots showing the results from measurements of spatial resolution as a function of position.

● Radial without range effects, ◆ tangential without range effects, ▲ axial without range effects, ○ radial with range effects, ◇ tangential with range effects, △ axial with range effects, ▴ radial with corrected range effects, □ tangential with corrected range effects and ■ axial with corrected range effects. (a) No photon acolinearity included in the simulations and (b) with photon acolinearity included.

Fig. 4.
Plot of slice sensitivity as a function of axial position of the source.

Fig. 5.
Coronal image of the microNEMA-NU4 Image Quality Phantom corrected for positron range.

Fig. 6. Plot of recovery coefficient as a function of rod diameter. The data were fit to a sigmoid function to guide the eye.

Fig. 7. TandemPET images of the micro-hot rod phantom. (a) Image without positron range correction (diameter of the rods are shown) and (b) image with positron range correction applied. The same intensity threshold (95% of maximum pixel value) was applied to both images.

Fig. 8.

TandemPET images of the brain section of the MOBY phantom. (a) MOBY phantom with major brain sections labeled (cortex (Cort), thalamus (Thal), hypothalamus (Hypo), caudoputamen (Caud), ventricles (Vent) (which contain no radioactivity) and amygdala (Amyg)), (b) simulated MicroPET® Focus 120 image of the MOBY phantom (c) TandemPET image of the MOBY phantom and (d) TandemPET image of the MOBY phantom corrected for positron range. The arrowheads highlight areas of increased separation of anatomy gained by high-resolution imaging and positron range correction (caudoputamen and amygdala). The same intensity threshold (95% of maximum pixel value) was applied to all images.

TABLE I

PEAK-TO-VALLEY RATIOS (PVR) MEASURED FROM THE IMAGES SHOWN IN FIG. 7.

Rod Diameter (mm)	PVR	
	Uncorrected	Corrected
1.0	2.2	4.1
0.8	1.5	2.4
0.6	1.2	1.5
0.5	1.1	1.2