Published in final edited form as:

IEEE Trans Radiat Plasma Med Sci. 2017 May ; 1(3): 262–267. doi:10.1109/TRPMS.2017.2682562.

Model-Based Normalization of a Fractional-Crystal Collimator for Small-Animal PET Imaging

Yusheng Li [Member, IEEE], Samuel Matej [Senior Member, IEEE], Joel S. Karp [Fellow, IEEE], and Scott D. Metzler [Senior Member, IEEE]

Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104 USA

Abstract

Previously, we proposed to use a coincidence collimator to achieve fractional-crystal resolution in PET imaging. We have designed and fabricated a collimator prototype for a small-animal PET scanner, A-PET. To compensate for imperfections in the fabricated collimator prototype, collimator normalization, as well as scanner normalization, is required to reconstruct quantitative and artifact-free images. In this study, we develop a normalization method for the collimator prototype based on the A-PET normalization using a uniform cylinder phantom. We performed data acquisition without the collimator for scanner normalization first, and then with the collimator from eight different rotation views for collimator normalization. After a reconstruction without correction, we extracted the cylinder parameters from which we generated expected emission sinograms. Single scatter simulation was used to generate the scattered sinograms. We used the least-squares method to generate the normalization coefficient for each LOR based on measured, expected and scattered sinograms. The scanner and collimator normalization coefficients were factorized by performing two normalizations separately. The normalization methods were also verified using experimental data acquired from A-PET with and without the collimator. In summary, we developed a model-base collimator normalization that can significantly reduce variance and produce collimator normalization with adequate statistical quality within feasible scan time.

Index Terms

Fractional-crystal collimation; Model-based normalization; crystal efficiencies; tomographic image reconstruction; positron emission tomography (PET)

I. INTRODUCTION

POSITRON emission tomography (PET) has become an important modality in medical and molecular imaging. In the past few decades the performance of PET systems has been substantially improved in terms of spatial resolution and sensitivity. However, in most preclinical PET applications, the resolution of PET scanners is still mainly limited by the physical sizes of the scintillator crystals or the intrinsic spatial resolution of the photon detectors [1]. For PET using discrete crystals, the empiric formula proposed by Moses and

Derenzo states that crystal width is one dominating factor for imaging resolution [2]. The most direct method is to reduce the crystal size (i.e. increase the number of crystals per unit area) by scintillator manufacturing techniques [3]–[5]. The reduction in crystal size can effectively improve the spatial resolution. However, it can be cost prohibitive with current manufacturing processes; there is increased inter-crystal scatters for smaller crystals; the small crystals can be under utilized for the general-purpose imaging applications. On the other hand, most current general-purpose PET scanners cannot provide the needed spatial resolution for specific regions-of-interest (ROI) imaging applications.

Previously, we proposed a fractional-crystal collimation approach to improve the transverse spatial resolution inside a central region of a PET scanner by adding a specially designed collimator [6]–[10]. The collimator runs the axial length of a PET scanner and has a translational symmetry axially. With the collimator, each detector crystal can be conceptually split into two sub-crystals by ‘masking’ the first or second half of the crystal with a high-density attenuator, e.g. tungsten; each crystal pair can measure 2×2 times as many resolution-enhanced LORs with four collimation combinations. Our collimator is designed to measure all interleaved LOR combinations by just rotating the collimator. Our collimated PET method can improve both linear and angular sampling, and especially, it can improve the transverse spatial resolution beyond the physical crystal size and detector intrinsic resolution. Obviously, there is a tradeoff among resolution, sensitivity and field of view (FOV). As a consequence of using the collimator, the geometric sensitivity of the collimated PET is approximately a quarter of that of the uncollimated PET. This may result in a longer scan time for some imaging scenarios that need more spatial information per photon [9], [11].

We have designed and fabricated a tungsten collimator prototype for A-PET, a small-animal PET scanner [12], [13]. We use A-PET as a testbed for our PET collimator to demonstrate the feasibility and performance advantage of the collimator. To efficiently utilize the collimated LORs, we developed an LOR-interleaving reconstruction algorithm dedicated to collimated PET, incorporating both detector and collimator modeling [11]. It is important to estimate normalization factor for each LOR and apply the normalization correction before or during image reconstruction for quantitative imaging [14], [15]. To compensate for imperfections in the fabricated collimator, collimator normalization, as well as scanner normalization, is required for the collimated PET to reconstruct quantitative and artifact-free images. The scanner normalization corrects the nonuniformity in LOR sensitivity including the intrinsic crystal efficiency, solid angle subtended and geometrical correction. Collimator normalization can correct imperfections in the fabrication of the prototype and the collimator attenuation. In this study, we have developed a procedure to estimate the collimator normalization coefficients and the scanner normalization coefficients using a uniform cylinder phantom. The collimator normalization combined with the scanner normalization can be incorporated into image reconstructions for collimated PET.

II. MATERIALS AND METHODS

A. Collimator Prototype and Experimental Setup

We have designed and fabricated a collimator prototype to improve the spatial resolution for a Philips Mosaic HP small-animal PET scanner (A-PET) [12], [13], as shown in Fig 1(a). We use A-PET as a testbed for our PET collimator prototype to demonstrate the feasibility and performance advantage of the collimator prototype. A-PET contains 278 LYSO crystals in a transverse ring with sizes of $2 \times 2 \times 10 \text{ mm}^3$, and there are 52 such rings along the axial direction. The transverse and axial crystal pitches are 2.34 mm and 2.31 mm, respectively. The scanner diameter is 19.7 cm with an axial length of 11.9 cm.

Our collimator prototype comprises 276 trapezoidal tungsten bars (front width 0.2 mm, back width 1.2 mm, length 140 mm). Each tungsten bar, registered to one axial column of crystals, can be configured transversely to expose either the first half (0) or the second half (1) of the crystals. The effective crystal width can be reduced from 2 mm to 1 mm for A-PET with the collimator prototype. The complete sampling of collimated LORs for each crystal pair requires the LORs between any two segments (not within a segment) be measured with four different ‘mask’ configurations, i.e., 00, 01, 10 and 11. We grouped the tungsten bars into eight segments which are respectively corresponding to crystals: 0–34, 35–69, 70–104, 105–138, 139–173, 174–208, 209–243, 244–277. The eight groups tungsten bars are configured as [0, 0, 0, 1, 1, 0, 1, 1], respectively. The two tungsten bars corresponding to crystals 104 and 209 were not installed due to the space limitation at segment boundaries, and these two uncollimated crystals in turn were used for collimator alignment. The collimator has a central efficiency FOV about 15 mm—the sweet spot where the collimator has the high and nearly uniform sensitivities [6]–[8].

The collimator prototype, attached to a motorized rotation stage (Model URS100PP, Newport Corporation, Irvine, CA), was placed inside the A-PET gantry as shown in Fig. 1(b). We installed eight ball bearings on the front and back ends of the collimator frame to rotate against the A-PET gantry. The collimator was rotated eight successive times in a step of about 45° for data acquisition; specifically, the collimator was rotated 0, 35, 70, 105, 139, 174, 209 and 244 crystals for the eight acquisitions [11].

To synchronize the collimator motion and PET data acquisition in real-time, we have developed a motion-acquisition synchronization technique. This technique allows us to automatically acquire list-mode data with different collimator rotations. We generated synchronized pulses using a digital I/O device (Model USB-6501, National Instruments Corporation, Austin, TX), and the pulses with different encoding patterns were sent to A-PET gating port as pseudo cardiac gating signals and recorded in list-mode data. The collimator status can be extracted by decoding the digital pulses in the pseudo cardiac control events. We used a motion controller (Model ESP300, Newport Corporation, Irvine, CA) to simultaneously control up to three motorized linear/rotation stages with synchronized motion. The digital I/O and motion controller are connected to a computer through USB and serial port, respectively. We developed a graphical user interface (GUI) using LabVIEW (National Instruments Corporation, Austin, TX) for the synchronized control of collimator motion and data acquisition.

B. Least-Squares Scanner Normalization

We used a uniform cylinder phantom filled with 2 mCi ^{18}F -FDG (diameter 10 cm, length 15 cm) for both data acquisitions with and without the collimator, as shown in Fig 1(c). The phantom was mounted to the animal table using a mounting bracket and placed near the center of the scanner (position error within 2 mm). We performed data acquisitions without the collimator for scanner normalization first, and then with the collimator from eight different rotation views for collimator normalization. For the scanner normalization, the LOR detection process for each ring combination is modeled as

$$d_j = s_{\text{true}} t_j + s_{\text{scat}} s_j + b, \quad j=0, \dots, n_\ell - 1, \quad (1)$$

where d_j is detected prompt events for LOR j , t_j and s_j are respectively true and scattered events, and n_ℓ is the number of LORs in a sinogram, s_{true} , s_{scat} and b are the detection scale for true events, the detection scale for scattered events and the background random events, respectively. The scatter sinograms were generated using single scatter simulation [16]. The true sinograms were generated from a mathematical cylinder with parameters estimated from a reconstruction without corrections. We performed the reconstruction without corrections using the row-action maximum likelihood algorithm (RAMLA) [17] to estimate the cylinder parameters including the centers and the axes of the cylinder with fixed diameter and axial length. Based on the estimated parameters we created cylinder activity and attenuation images and then used ray-tracing to generate the true emission and attenuation sinograms from respectively the uniform activity and attenuation images. The three parameters (true scale, scatter scale and background offset) for each ring combination can be estimated simultaneously using the least-squares method as

$$\begin{bmatrix} \hat{s}_{\text{true}} \\ \hat{s}_{\text{scat}} \\ \hat{b} \end{bmatrix} = M^{-1} \begin{bmatrix} \sum_{j=0}^{n_\ell-1} t_j d_j \\ \sum_{j=0}^{n_\ell-1} s_j d_j \\ \sum_{j=0}^{n_\ell-1} d_j \end{bmatrix}, \quad (2)$$

where

$$M = \begin{bmatrix} \sum_{j=0}^{n_\ell-1} t_j^2 & \sum_{j=0}^{n_\ell-1} s_j t_j & \sum_{j=0}^{n_\ell-1} t_j \\ \sum_{j=0}^{n_\ell-1} s_j t_j & \sum_{j=0}^{n_\ell-1} s_j^2 & \sum_{j=0}^{n_\ell-1} s_j \\ \sum_{j=0}^{n_\ell-1} t_j & \sum_{j=0}^{n_\ell-1} s_j & n_\ell \end{bmatrix}. \quad (3)$$

Based on the estimated scales, the normalization coefficient η_j for LOR j can be determined as

$$\eta_j = \frac{s_{\text{model}}}{d_j} \left(t_j + \frac{\hat{s}_{\text{scat}}}{\hat{s}_{\text{true}}} s_j + \frac{\hat{b}}{\hat{s}_{\text{true}}} \right), \quad (4)$$

where

$$s_{\text{model}} = \langle d \rangle / \left(\langle t \rangle + \frac{\hat{s}_{\text{scat}}}{\hat{s}_{\text{true}}} \langle s \rangle + \frac{\hat{b}}{\hat{s}_{\text{true}}} \right). \quad (5)$$

Here the angle brackets denote statistical averaging over all LORs within a ring combination.

Since the LORs outside the object can only be considered as scattered or random events, an alternative to the simultaneously estimating of the three parameters is to estimate them in two steps. First, the scatter scale and background offset can be estimated using the LOR events outside the object boundary, and then the true scale can be estimated using the LORs inside the object by segmenting the sinograms. The Casey average was used to reduce the variance for the estimated scanner normalization coefficients [18], [19].

C. Model-Based Collimator Normalization

For collimator normalization, we developed a model-based variance reduction technique dedicated for the collimator normalization. As shown in Fig. 2, the collimator attenuation and imperfection of the tungsten bars for the 3-D collimated PET can be factorized and modeled as

$$\eta[r, \phi, z_1, z_2] = C w[x_1(r, \phi)] w[x_2(r, \phi)] e^{-\mu L[r] \sec \theta}, \quad (6)$$

where $\sec \theta = \sqrt{R^2 - s^2 + \Delta^2/4} / \sqrt{R^2 - s^2}$ and ϕ define a LOR's radial and angle indices in the transverse view, Δ is the axial spacing between the two crystals, $L[r] \sec \theta$ is the effective intersection length between the LOR and the collimator, $s = s[r]$ is the distance between the $\hat{z}$ axis and the projection of the LOR onto a transverse plane, R is the scanner radius, μ is the linear attenuation coefficient of the collimator material tungsten, and C is a multiplication constant. The two back-to-back gamma rays from an annihilation event can penetrate through the tungsten collimator and be detected by a pair of crystals. We use $w[x]$ to model collimator nonuniformity at the crystal x due to the tungsten bar imperfection in the fabricated collimator prototype (independent of z because of its axial symmetry). For an LOR connected by two crystals (x_1, z_1) and (x_2, z_2) , the factor is $w[x_1]w[x_2]$. Without loss of generality, we assume that the constant C is absorbed by the term w . By taking the logarithm, we have a vectorized model as

$$\log \eta[r, \phi, z_1, z_2] = \log w[x_1] + \log w[x_2] - \mu L[r] \sec \theta = [\mathbf{A} \log \mathbf{w}]_{(r, \phi)} - \mu L[r] \sec \theta, \quad (7)$$

where $A_{(r, \phi), x} = 1$ when LOR (r, ϕ) intersects with crystal x and 0 otherwise (it has two ones in each row), and $\log \mathbf{w}$ is a column vector whose x -th element is $\log \mathbf{w}[x]$. Here we took a natural logarithm to make a linear model with respect to the parameters $\log \mathbf{w}$, which is similar to the logarithm taken in computed tomographic (CT) image reconstruction.

Because the collimator is axially symmetric, we can compute the average of (7) over the axial indices (z_1, z_2) to reduce the variance in the estimated collimator parameters. By taking the double average over n_z axial crystals, we have

$$-[\mathbf{A} \log \mathbf{w}]_{(r, \phi)} + \mu L[r] P[r] = T[r, \phi], \quad (8)$$

where

$$P[r] = \frac{1}{n_z^2} \sum_{z_1=0}^{n_z-1} \sum_{z_2=0}^{n_z-1} \sec \theta, \quad (9)$$

$$T[r, \phi] = -\frac{1}{n_z^2} \sum_{z_1=0}^{n_z-1} \sum_{z_2=0}^{n_z-1} \log \eta[r, \phi, z_1, z_2]. \quad (10)$$

By changing variables $z = \frac{z_1 + z_2}{2}$ and $d_z = z_1 - z_2$, we can further simplify $P[r]$ as:

$$P[r] = \frac{1}{n_z^2} \sum_{d_z=-n_z+1}^{n_z-1} \sum_{z=|d_z|/2}^{n_z-1-|d_z|/2} \sec(\theta[d_z]), \quad (11)$$

$$= \frac{1}{n_z^2} \sum_{d_z=0}^{n_z-1} (2 - \delta[d_z]) (n_z - |d_z|) \sec \theta, \quad (12)$$

$$\hat{L}^{(n+1)}[r] = \frac{1}{\mu P[r] n_\phi} \sum_{\phi=0}^{n_\phi-1} \left([\mathbf{A} \log \hat{\mathbf{w}}^{(n)}]_{(r, \phi)} + T[r, \phi] \right), \quad (13)$$

$$\log \hat{\mathbf{w}}^{(n+1)} = \arg \min_{\log \mathbf{w}} \left(\text{vec} \left(-T[r, \phi] + \mu \hat{L}^{(n+1)}[r] P[r] \right), \mathbf{A} \log \mathbf{w} \right). \quad (14)$$

where $\delta[d_z]$ is the Kronecker delta function of discrete variable d_z i.e., $\delta[0] = 1$ and $\delta[d_z] = 0$ for $d_z \neq 0$.

Next, we focus on solving (8) with two sets of unknowns: the collimator nonuniformity $\mathbf{w}$ and the effective intersection lengths $L[r]$, $r = 0, 1, \dots, n_r - 1$. We use n_r and n_ϕ to denote the number of rays and the number of angles in a LOR sinogram, respectively. For A-PET, the LOR sinogram is binned into $125 \text{ rays} \times 139 \text{ angles}$. Similar to the maximum-likelihood reconstruction of attenuation and activity (MLAA) [20], we use an alternating iterative algorithm to solve the two sets of unknown parameters. In each iteration, the effective intersection lengths $L[r]$ are updated while keeping the current values for the collimator nonuniformity $\mathbf{w}$, and then vice versa. The alternating iterative algorithm for collimator normalization is given in (13) and (14). Here, we use $\mathcal{D}(\mathbf{p}, \mathbf{q})$ to denote a distance measure between vectors $\mathbf{p}$ and $\mathbf{q}$, and $\text{vec}(\cdot)$ to denote a vectorization operation which converts its argument (a matrix) into a column vector. The Euclidean distance and Kullback-Leibler (KL) divergence are often used for the distance measure, and the least-squares method and MLEM can be used respectively to solve the collimator nonuniformity $\mathbf{w}$ in (14). Due to the axial symmetry of the collimator, we used factor $w[x]$ to model the tungsten bar nonuniformity. One can extend the normalization method to the collimators designed without axial symmetry by using $w[x, z]$ to model the collimator nonuniformity. It is worth noting that the nonuniformity factors are positive numbers, and this is a natural constraint in $\log$. One can also constrain the solution $\mathbf{w} \geq 1$, by applying the constraint of the nonnegative unknowns $-\log \mathbf{w}$ in (14).

III. RESULTS

A. Scanner Normalization

For scanner normalization, we filled the uniform cylinder phantom with 2 mCi ^{18}F -FDG and collected a total of 4.60 billion events in the LOR sinogram format. We performed a reconstruction without any correction using the LORs with maximum ring difference of 2. The RAMLA algorithm with 2 iterations was used for the uncorrected reconstruction [17]. From the 3-D reconstructed image we estimated the cylinder parameters (the center and the axes of the cylinder) with fixed diameter 10 cm and axial length 15 cm. Based on the estimated parameters, we created activity and attenuation images, and then generated true emission and transmission sinograms using ray-tracing of the mathematical cylinder with the estimated parameters. The linear attenuation coefficient for water at 511 keV is 0.095 cm^{-1} . The scatter sinograms were generated using single scatter simulation [16]. Based on measured, true and scattered sinograms, we computed true scale, scatter scale and background offset for each sinogram using the least squares method (2), and the normalization coefficients were computed using (4). To reduce the variance, the Casey average was applied to estimated scanner normalization coefficients [18], [19]. The data sinogram acquired from the uniform cylinder phantom is shown in Fig. 3(a), and the corresponding estimated scanner normalization sinogram is shown in Fig. 3(b).

B. Collimator Normalization

We aligned the collimator before performing the normalization acquisition using a ^{22}Na source. Thanks to the motion-acquisition synchronization technique, we automatically rotated the collimator with very high precision. The collimator has four gaps between different configurations (the corresponding crystals have high sensitivity). We rotated the collimated 21 steps in a step of 0.1295° (corresponding to 0.1 crystal pitch), and aligned the collimator by computing the correlation function of the crystal responses. We refilled the uniform cylinder phantom with the same activity of 2 mCi ^{18}F -FDG, and we collected a total of 660 million counts of list-mode data from eight rotation views for the collimator normalization. We tested the model-base collimator normalization method using simulated data by ray-tracing of the collimator [11], and it worked well in both fitting the simulated data and reducing variance. We then applied the collimator normalization method to the experimentally acquired data.

We used the scanner normalization as a prior in estimating the collimator normalization. The total normalization is a product of scanner normalization and collimator normalization. By factoring out the scanner normalization, we can further reduce the variance for the collimator normalization using model (6). We used the alternating iterative algorithm (13) and (14) with iteration number 512 to estimate the collimator parameters, and the least squares method was used for (14) in estimating the collimator nonuniformity. Fig 4 shows the data sinogram acquired from the cylinder phantom, the corresponding computed collimator normalization sinogram, and the total normalization sinogram (the product of scanner and collimator normalization sinograms). The collimator normalization sinogram is low at the center FOV where the collimator has high sensitivity. We can see that the model-base collimator normalization fitting can significantly reduce variance and produce collimator normalization with good statistical quality at feasible scan time.

C. Verification

For verification, we performed image reconstruction of the uniform cylinder phantom (diameter 10 cm, length 15 cm). The reconstructed images without normalization correction, with only scanner normalization correction and with both scanner and collimator normalization corrections are shown in Fig. 5. The reconstructed images are $128 \times 128 \times 120$ with voxel size of 1 mm. The RAMLA algorithm with 8 iterations was used. Attenuation correction, random and scattered events correction were applied during the image reconstruction. Due to the collimation, the detected scattered events were much fewer than those of the uncollimated case. The scatter sinogram was estimated from the data sinogram with delayed-events subtracted after both scanner and collimation normalizations based on the single scatter simulation model [16]. From the reconstructed images, we can see that the nonuniformity of scanner and collimator prototype, as well as the collimator attenuation, can be corrected after applying the normalization corrections. There is still some residual nonuniformity near the center of the reconstructed images in Fig. 5(c), which might be caused the residual error in the scatter estimation. The bright central regions in the top row of Fig. 5(a) and Fig. 5(b) indicate the efficiency field of view of the collimator prototype [11].

To quantify the uniformity of collimated reconstructions, we computed the mean and standard deviation values of the reconstruction images in a central cylinder region and in a peripheral annulus region. The central cylinder region has diameter of 15 mm and height of 20 mm, which is the sweet spot of the collimator. The diameters of the annulus region are 40 mm and 80 mm, and the height is 20 mm. The ratio of the means between the central region and peripheral region are 4.63, 5.29 and 0.953 for the three cases of without normalization, with scanner normalization and with both scanner and collimator normalizations, respectively. The %STD (standard deviation divided by mean) in the central region are respectively 22.61 %, 22.44 % and 13.09 % for the three cases; and the %STD in the peripheral region are respectively 12.28 %, 13.96 % and 12.74 % for the three cases.

IV. DISCUSSION AND CONCLUSION

We developed the model-based normalization method for our collimator prototype designed for a small-animal PET scanner, A-PET, with cylindrical geometry. The method takes both the detection efficiency as well as the collimation efficiency into account, i.e., the total normalization is the product of scanner normalization and the collimator normalization. The method is an extension of the routine A-PET normalization procedure, and the scanner normalization is essentially the same as the routine normalization without collimation. A scanner normalization is required for quality control at a routine interval (e.g., quarterly, or semiannually). To acquire the scanner normalization, the collimator would have to be removed and replaced afterwards with high reproducibility. To ensure the high reproducibility of the collimation replacement, a quick data acquisition is required to properly align the collimator. Theoretically, the collimator normalization would not change. However, we may repeat the collimator normalization after each scanner normalization in order to account for any non-reproducibility of collimator replacement.

The method can also be extended to other special collimators designed for clinical PET scanners with polygon geometry, or dedicated PET scanners with special geometries, by applying the collimator symmetries. The least squares method in (14) can also be applied to other imaging applications, e.g., to estimate the time-variant crystal efficiencies in PETMR using avalanche photodiodes (APDs), because APD's efficiency is very sensitive to operating temperature [21]. A drawback of this model-based approach is that the accuracy of the normalization is dependent on the accuracy of the model used to describe the collimator. However, it has the advantage that a more intelligent treatment of the different properties of different components is possible. The scanner normalization may change over time, while the collimator normalization usually does not. So, the collimator normalization can be estimated only once from the measured collimated data with high statistics. This is analogous to the component-based methods for scanner normalization [14], [15]—specifically, some scanners use this technique to measure the effects of detector geometry (e.g., for a block detector) once and then fold these into the overall efficiency correction which include variations due to PMT gain drift, time-variant crystal efficiencies, etc. The depth-of-interaction (DOI) is not included in the model, which might cause slight blur in the estimated normalization coefficients. This blur error is very small compared to the noise in the data. And we demonstrated the usefulness of the normalization method.

In summary, we have developed a model-based normalization method to correct collimator effects, which allows quantitative and artifact-free reconstructions for the collimated PET. The normalization method can generate collimator normalization coefficients with significantly reduced variance at feasible scan time. We demonstrated the normalization method can effectively correct the imperfections in the fabricated collimator prototype, as well as the collimator attenuation, and produce accurate reconstructed images after normalization for the collimated PET. Future works, including extension of the collimator model, precise collimator fabrication, and resolution phantom studies, are required to fully explore the potential of the collimated PET.

Acknowledgments

We would like to thank Mr. Eric Blankemeyer for help on data acquisition with A-PET scanner, Mr. Matthew Werner for providing software and computing assistance. We would like to acknowledge Mr. William Pennie from Research Instrumentation Shop for machining the frame of the collimator prototype. Finally, the tungsten bars were machined by Tungsten Heavy Powder (San Diego, CA), and the collimator fixtures were printed by Forecast 3D (Carlsbad, CA). Research reported in this publication was supported in part by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH) under award number R21EB12158. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Stickel JR, Cherry SR. High-resolution PET detector design: modelling components of intrinsic spatial resolution. *Phys Med Biol.* Jan; 2005 50(2):179–195. [PubMed: 15742938]
2. Moses WW, Derenzo SE. Empirical observation of resolution degradation in positron emission tomographs utilizing block detectors [abstract]. *J Nucl Med.* 1993; 34:101P.
3. Cherry S, Shao Y, Silverman R, et al. MicroPET: A high resolution PET scanner for imaging small animals. *IEEE Trans Nucl Sci.* Jun; 1997 44(3):1161–1166.
4. Miyaoka RS, Kohlmyer SG, Lewellen TK. Performance characteristics of micro crystal element (MiCE) detectors. *IEEE Trans Nucl Sci.* Aug; 2001 48(4):1403–1407.
5. Yang Y, St James S, Wu Y, Du H, Qi J, Farrell R, Dokhale PA, Shah KS, Vaigneur K, Cherry SR. Tapered LSO arrays for small animal PET. *Phys Med Biol.* Jan; 2011 56(1):139–153. [PubMed: 21119228]
6. Li Y, Metzler SD. Resolution enhanced PET using collimation [abstract]. *J Nucl Med.* 2012; 53(S1): 2396.
7. Li, Y., Matej, S., Karp, JS., Metzler, SD. IEEE NSS/MIC. Anaheim, CA: 2012. System design considerations for collimation in a small-animal PET scanner; p. 2838–2842.
8. Li Y, Matej S, Karp J, Metzler S. Design and integration of a collimator prototype to achieve fractional-crystal resolution in a small-animal PET system [abstract]. *J Nucl Med.* 2013; 54(S2): 597.
9. Metzler SD, Matej S, Karp JS. Resolution enhancement in PET reconstruction using collimation. *IEEE Trans Nucl Sci.* Feb; 2013 60(1):65–75. [PubMed: 23493920]
10. Li, Y., Matej, S., Karp, JS., Metzler, SD. IEEE NSS/MIC. Seoul, Korea: 2013. Model-based normalization of a fractional-crystal collimator prototype for small-animal PET imaging.
11. Li Y, Matej S, Karp JS, Metzler SD. LOR-interleaving image reconstruction for PET imaging with fractional-crystal collimation. *Phys Med Biol.* Jan; 2015 60(2):647–670. [PubMed: 25555160]
12. Surti S, Karp JS, Perkins AE, Freifelder R, Muehllehner G. Design evaluation of A-PET: A high sensitivity animal PET camera. *IEEE Trans Nucl Sci.* Oct; 2003 50(5):1357–1363.
13. Surti S, Karp JS, Perkins AE, Cardi CA, Daube-Witherspoon ME, Kuhn A, Muehllehner G. Imaging performance of A-PET: A small animal PET camera. *IEEE Trans Nucl Sci.* Jul; 2005 24(7):844–852.

14. Badawi RD, Marsden PK. Developments in component-based normalization for 3D PET. *Phys Med Biol.* Feb; 1999 44(2):571–594. [PubMed: 10070802]
15. Bai B, Li Q, Holdsworth C, Asma E, Tai YC, Chatziioannou A, Leahy RM. Model-based normalization for iterative 3D PET image reconstruction. *Phys Med Biol.* Aug; 2002 47(15):2773–2784. [PubMed: 12200938]
16. Watson CC. New, faster, image-based scatter correction for 3D PET. *IEEE Trans Nucl Sci.* Aug; 2000 47(4):1587–1594.
17. Browne J, De Pierro AR. A row-action alternative to the EM algorithm for maximizing likelihoods in emission tomography. *IEEE Trans Med Imag.* Oct; 1996 5(5):687–699.
18. Casey ME, Hoffman EJ. Quantitation in positron emission computed tomography: 7. A technique to reduce noise in accidental coincidence measurements and coincidence efficiency calibration. *J Comput Assist Tomogr.* Sep; 1986 10(5):845–850. [PubMed: 3489018]
19. Meikle, SR., Badawi, RD. Quantitative techniques in PET. In: Bailey, DL.Townsend, DW.Valk, PE., Maisey, MN., editors. *Positron Emission Tomography: Basic Sciences*. Berlin: Springer; 2005. p. 93-126.
20. Nuyts J, Dupont P, Stroobants S, Benninck R, Mortelmans L, Suetens P. Simultaneous maximum a posteriori reconstruction of attenuation and activity distributions from emission sinograms. *IEEE Trans Med Imag.* May; 1999 18(5):393–403.
21. Belzunce MA, Reader AJ. Time-invariant component-based normalization for a simultaneous PET-MR scanner. *Phys Med Biol.* May; 2016 61(9):3554–3571. [PubMed: 27054290]

Fig. 1.

The fabricated tungsten collimator prototype, attached to a motorized rotation stage, was placed inside the A-PET gantry from the opposite side of the animal table for data acquisition. The uniform cylinder phantom was mounted to the animal table using a mounting bracket for the scanner and collimator normalization. (a) The collimator prototype. (b) Experimental setup. (c) Uniform cylinder phantom.

Fig. 2.

Geometry of the 3-D collimated PET. Transverse view (left) with LOR sinogram indices (r , ϕ). Longitudinal section (right) with the axial indices (z_1 , z_2). Note that the axes $\hat{x}$ and $\hat{y}$ axis are rotated for illustrative purposes.

Fig. 3. Representative data sinogram acquired from the uniform cylinder phantom without the collimator prototype (a), and the corresponding estimated scanner normalization sinogram (b).

Fig. 4.

Representative data sinogram acquired from the uniform cylinder phantom with the collimator prototype (a), the corresponding estimated collimator normalization sinogram (b), and the total normalization sinogram, i.e., the product of scanner and collimator normalization sinograms (c).

Fig. 5.

Reconstructed images of the uniform cylinder phantom without normalization (a), with only scanner normalization (b), and with both scanner and collimator normalization (c). The top row shows the transverse images and the bottom shows the coronal images