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A novel depth-of-interaction rebinning strategy for ultrahigh resolution PET

Kyungsang Kim¹, Joyita Dutta^{1,2}, Andrew Groll³, Georges El Fakhri¹, Ling-Jian Meng³, and Quanzheng Li¹

¹Gordon Center for Medical Imaging, Massachusetts General Hospital and Harvard Medical School.

²Department of Electrical and Computer Engineering, University of Massachusetts Lowell.

³Department of Nuclear, Plasma and Radiological Engineering, University of Illinois.

Abstract

Small animal PET imaging often requires high resolution (~ few hundred microns) to enable accurate quantitation in small structures such as animal brains. Recently, we have developed a prototype ultrahigh resolution depth-of-interaction (DOI) PET system that uses CZT detectors with a detector pixel size of 350 μm and 8 DOI layers with a 250 μm depth resolution. Due to the large number of line-of-response (LOR) combinations of DOIs, the system matrix for reconstruction is 64 times larger than that without DOI. While a high resolution virtual ring geometry can be employed to simplify the system matrix and create a sinogram, the LORs in such a sinogram tend to be sparse and irregular, leading to potential degradation of the reconstructed image quality. In this paper, we propose a novel high resolution sinogram rebinning method in which a uniform sub-sampling DOI strategy is employed. However, even with the high resolution rebinning strategy, the reconstructed image tends to be very noisy due to insufficient photon counts in many high resolution sinogram pixels. To reduce noise effects, we developed a penalized maximum likelihood reconstruction framework with the Poisson log-likelihood and a non-convex total variation (TV) penalty. Here, an ordered subsets separable quadratic surrogate (OS-SQS) and alternating direction method of multipliers (ADMM) are utilized to solve the optimization. To evaluate the performance of the proposed sub-sampling method and the penalized maximum likelihood reconstruction technique, we perform simulations and preliminary point source experiments. By comparing the reconstructed images and profiles based on sinograms without DOI, with rebinned DOI (rDOI) and with sub-sampled DOI (sDOI), we demonstrate that the proposed method with sub-sampled DOIs can significantly improve the image quality with lower dose and yield a high resolution of $< 300 \mu\text{m}$.

1. Introduction

Small animal positron emission tomography (PET) is widely used to study animal models of human disease (Kemp et al. 2010), which can not only facilitate our understanding of biomolecular pathways but also the accelerate the development of new drugs and biomarkers. However, compared to human clinical scanners, the resolution of state-of-the-art small animal scanners is rather limited for their target applications. For example, the striatum is a brain structure that can be easily visualized in humans using a state-of-the-art

clinical PET scanner, however, visualization of the striatum in a mouse brain requires sub-millimeter resolution, which is beyond the capabilities of current small-animal PET scanners. The resolution of the animal scanner is required at least sub-millimeter resolution range

In conventional PET scanners, the parallax error (detector positioning error due to the photon penetration through multiplecrystal elements) produces blurring artifacts, which severely affects the image resolution of small animal PET scanners due to the larger parallax error caused by smaller ring geometry. To overcome this challenge and increase the spatial resolution, reconstruction-based approaches have been successfully developed. Specifically, an accurate system matrix based on the spatially-variant point spread function (PSF) was used in iterative reconstruction (Qi et al. 1998, Tohme & Qi 2009, Reader et al. 2003). An alternative hardware-based approach is to use a depth-of-interaction (DOI) detector that can significantly reduce the parallax error. DOI detectors have been used in several commercialized PET scanners. The high resolution research tomograph (HRRT) (Wienhard et al. 2002) was the first DOI-PET scanner with two DOI layers providing up to 1.2 mm image resolution. More advanced DOI-PET scanners using half detector element shift of DOI layers have been developed for higher resolution in small animal PET (Mizuta et al. 2008, Ito et al. 2011).

Although the conventional scintillator-based detectors for small animal PET scanners with DOI are well-developed, sub-millimeter resolution is still technically difficult (Yang et al. 2012). Recently, alternative directions have emerged based on semiconductor detectors, such as silicon, CdTe and CdZnTe (CZT), which allows excellent energy and spatial resolutions as well as detection efficiency (Gu et al. 2011). There has been significant effort towards building ultrahigh resolution PET scanner using CdTe and CZT detectors (Matteson et al. 2008, Yang et al. 2012, Mitchell et al. 2008, Morimoto et al. 2011, Ueno et al. 2009, Macias-Montero et al. 2013, Yin et al. 2014).

In our previous studies (Groll et al. 2015, Groll et al. 2016, Groll et al. 2017), we have developed a hybrid pixel-waveform (HPWF) CZT/CdTe detector design that can offer an ultrahigh intrinsic spatial resolution with a detector pixel of $350\ \mu\text{m}$ as shown in figure 1. In the prototype scanner, two detector panels and a rotating object, as shown in figure 1(a), are used to emulate the full-ring system. To achieve ultrahigh resolution, the DOI encoding has a great role by packing additional detector layers for more accurate positioning. However, the DOI information dramatically increases not only the data size but also the system matrix size. k DOIs increases the data size by a factor of k^2 compared to the conventional sinogram without DOI. Specifically, our prototype has 8 DOIs as shown in figure 1(b), which requires a 64 times larger system matrix for reconstruction compared to without DOI, which poses a major computational challenge.

To reduce the data size with DOIs, a virtual ring detector geometry has been utilized, in which the lines of response (LORs) of DOI bins are projected onto the front DOI bins (Yamaya et al. 2002, Yamaya et al. 2008). Zhang *et al.* developed a small animal PET scanner with three DOI layers and successfully utilized a virtual detector containing gaps representing the unmeasured area between the two detector panels (Zhang et al. 2015). Here,

the optimal resolution of virtual detector was slightly higher than the half of real crystal size. Groll *et al.* (Groll et al. 2017) have exploited the same virtual detector sinogram rebinning using the ordered subsets expectation maximization (OSEM) algorithm and modeling the point spread function (PSF) to achieve a resolution of 30% higher than half of the actual crystal size.

In this paper, we are interested in both reducing the data size and achieving higher resolution for our DOI PET scanner. For reducing the data size, we exploit a virtual detector geometry with a novel rebinning strategy that ensures higher rebinning resolution to exploit the full strength of the large number of DOI layers. We tackle two major issues related to high resolution rebinning: 1) irregularity of LORs and 2) decision of optimal resolution for the virtual detector in the rebinning process. More specifically, due to the different resolutions of the detectors along the radial and transaxial directions, conventional rebinned DOI (rDOI) leads to sparse and irregular sampling, which can potentially degrade the image quality, as shown in figure 2(a). Additionally, it is critical to determine the optimal resolution for rebinning so as to curb computational costs without sacrificing ultrahigh resolution performance. To address the first issue, we propose a sub-sampling DOI (sDOI) rebinning scheme by employing uniform sub-sampling grids along both width and depth directions in each detector as shown in figure 2(b). By promoting regular grid sampling, the sinogram quality becomes more stable despite the increase in the virtual detector resolution. For validation, we will compare performances of reconstructed images using sinogram without DOI, with conventional rebinned DOI (rDOI) in figure 2(a), and with proposed sub-sampling DOI (sDOI) in figures 2(b)(c). Axial sub-sampling based on virtual detector is more accurate compared to conventional ring differences as shown in figure 2(c).

Furthermore, insufficient photon counts in small virtual detector bins also lead to higher noise levels, which, in turn, necessitates higher radiotracer doses for small animal experiments. To address this issue, we propose a penalized maximum likelihood reconstruction technique that utilizes an ordered subsets separable quadratic surrogates (OS-SQS) algorithm for the Poisson log-likelihood and alternating direction method of multipliers (ADMM) algorithm for a non-convex total variation (TV) penalty incorporated to reduce the noise while preserving edge structures. We also implemented De Pierro's penalized OSEM (De Pierro 1994) with L1-based TV for comparison.

To validate the proposed rebinning and reconstruction methods, we first simulate an 8-DOI geometry that is exactly the same as our prototype, and perform Monte Carlo simulations using a resolution phantom. Normalized root mean square error (NRMSE), bias, and structural similarity (SSIM) index were the three figures of merit used for quantitation. In real data experiment, we used a point source with a 250 μm diameter and the Na-22 radioisotope. Using a single point source, we generate multiple datasets for point source based resolution assessments. More specifically, by controlling the initial angle of geometry and adding data with different rotation angles, data based on multiple point sources at different locations can be acquired. Using simulations and experiments, we demonstrate that reconstructed image using the sDOI method is robust to intrinsically low photon statistics and sub-300 μm can be achieved.

2. Methods

2.1. Configuration of prototype scanner

The small-pixel CZT based prototypic PET system has been reported in (Meng et al. 2009) based on the energy resolvable photon counting (ERPC) detectors with an ultra-compact design as shown in figure 1. Each pixel element is $350\ \mu\text{m} \times 350\ \mu\text{m}$ with 2 mm radial thickness. A rotational motor is used to simulate a detector ring, and the detector can provide a DOI resolution of $250\ \mu\text{m}$. The distance between the two detector panels is 34 mm. Data is acquired by rotating the object in 40 angular steps uniformly distributed along a circle.

2.2. Sinogram rebinning

2.2.1. High-resolution virtual detector—The size of the geometric component of the system matrix with DOIs is significantly larger than that without DOI because of the large number of potential LORs with multiple DOI combinations. For example, if we have k DOI layers, it is virtually equivalent to a traditional system with k concentric detector rings. Therefore, the number of detector ring combinations is k^2 in the LOR space, and the system matrix with DOI is k^2 times larger than that without DOI. To reduce the size of the system matrix and simplify the geometric model, we utilized a high resolution virtual detector geometry. More specifically, the virtual detector has a single layer with $< 300\ \mu\text{m}$ resolution (a detailed discussion on optimal rebinning resolution will be presented in Section 3) and coincides with the first DOI layer on the real system, which can reduce the data and system matrix sizes significantly. For example, if the resolution is $50\ \mu\text{m}$, the data and system matrix size are only 3.5 times larger than those for a 1-DOI system whose optimal resolution of $175\ \mu\text{m}$ is half of the detector size. However, the data size of 8-DOIs is 64 times larger than the size of 1-DOI, thus the proposed high resolution virtual detector can significantly reduce the data and system matrix sizes. For each LOR in the DOI layers, we compute the projection on the surface of the virtual detector as shown in figure 2, and then collect coincidences corresponding to high resolution virtual detectors.

2.2.2. Sub-sampling method—Although the virtual detector ring significantly reduces the computational complexity, the data sampling in the sinogram space can be sparse and irregular as shown in figure 2(a), which could potentially degrade the reconstructed image quality. To address this issue, we also divide the detector into high-resolution sub-detectors along the width and depth directions as shown in figure 2. We used a uniform sub-detector size for regular sampling with the sub-detector resolution assumed to be same as the resolution of the virtual detector. This strategy effectively divides each LOR into multiple sub-LORs, which reduces the sinogram entries (LORs) with missing data and thereby reduces the sparseness of the high resolution sinogram.

2.3. Normalization

Our prototype scanner has only two detector panels that rotate with 40 angular shifts. Our normalization operation considers the detector sensitivity between the two panels and decay correction for the time dependent angular shifts. We first virtually create a large cylinder with uniform activity. A normalization measurement with sufficient coincidence events based on a Monte Carlo simulation is generated. The decay correction factor is multiplied

directly with the data of each angle. The resultant correction factors are used to normalize the sinogram before reconstruction.

2.4. Formulation

A non-negative image $x = (x_1, \dots, x_{N_v}) \in \mathbb{R}_+^{N_v}$ is reconstructed from a measurement $y = (y_1, \dots, y_{N_m}) \in \mathbb{R}_+^{N_m}$. Here, N_v and N_m denote the numbers of image voxels and sinogram bins, respectively. y is the number of photon counts including true, scatter and random coincidence events in the sinogram including DOI information. PET data follows a Poisson statistical model:

$$y_i \sim \text{Poisson} \{ [Ax]_i + r_i \}, \quad (1)$$

where y_i is the number of counts in the i th sinogram bin. r_i is the estimated value of scatter and random events (Humm et al. 2003) with the i th sinogram bin. $A \in \mathbb{R}_+^{N_m \times N_v} = BP$ is the system matrix composed of sinogram blurring matrix (B) based on the point spread function (PSF) and the virtual geometrical projection matrix P . $[Px]_i = \sum_{j=1}^{N_v} a_{ij} x_j$ represents the line integral along a line of response (LOR) and a_{ij} denotes the probability in which a pair of photons emitted from the j th voxel is detected at the i th sinogram bin. In the absence of PSF modeling, B denotes the identity matrix.

In this paper, we minimize the following cost function $\Psi_o(x)$:

$$\Psi_o(x) = L(x) + \beta R(x), \quad (2)$$

where $L(x) = \sum_{i=1}^{N_m} h_i([Ax]_i)$ denotes the negative log-likelihood function from the Poisson statistics, and $h_i(k) = k + r_i y_i \log(k + r_i)$. $R(x)$ is the generalized Huber-based total variation (Goldstein & Osher 2009) that controls the noise variance of the reconstructed image while preserving edge structures. Here, $\beta > 0$ is a hyper-parameter.

2.5. Optimization

2.5.1. SQS—To minimize the cost function, we use a majorizer of $L(x)$ using separable quadratic surrogates (SQS) (Erdogan & Fessler 1999):

$$L(x) \leq \phi_L^{(n)}(x) \triangleq \sum_{j=1}^{N_v} \phi_{L,j}^{(n)}(x_j), \quad (3)$$

and

$$\phi_{L,j}^{(n)}(x_j) \triangleq \sum_{i=1}^M g_{ij} p_i^{(n)} \left(\frac{a_{ij}}{g_{ij}} (x_j - x_j^{(n)}) + [Ax^{(n)}]_i \right), \quad (4)$$

where $g_{ij} = \frac{a_{ij}}{\sum_{j'=1}^N a_{ij'}}$ is a non-negative real value ($g_{ij} = 0$ only if $a_{ij} = 0$ for all i, j), and

$$p_i^{(n)}(k) \triangleq h_i(k_i^{(n)}) + \dot{h}_i(k_i^{(n)})(k - k_i^{(n)}) + \frac{v_i^{(n)}}{2}(k - k_i^{(n)})^2, \quad (5)$$

where $k_i^{(n)} = [Ax^{(n)}]_i$ at n th iteration, and $v_i^{(n)}$ is the curvature of $p_i^{(n)}(k)$, in which we used the precompute curvature $1/\max(v_i, \epsilon)$ for the computational efficiency. $\epsilon = 10^{-9}$ is a small positive constant. In addition, we use the ordered subsets version of SQS (OS-SQS) in this project for fast convergence (Erdogan & Fessler 1999).

2.5.2. ADMM with OS-SQS and TV—In this paper, instead of using the L_1 norm, we used the non-convex total variation (TV) with the Huber function. Specifically, $R(x) = \|Rx\|_{h(\mu, \nu)}$, where $h_{\mu, \nu}(l)$ is a generalized Huber function defined as:

$$h_{\mu, \nu}(l) = \begin{cases} |l|^2/2\mu, & \text{if } |l| < \mu^{1/(2-\nu)} \\ |l|^\nu/\nu - \delta, & \text{if } |l| \geq \mu^{1/(2-\nu)} \end{cases} \quad (6)$$

where $\delta = (1/\nu - 1/2)\mu^{\nu/(2-\nu)}$ to make the function continuous and differentiable. Rx is the 3D gradient operator of x , such as ∇_x, ∇_y and ∇_z .

The generalized Huber function is convex when $\nu = 1$ and non-convex $\nu < 1$ (Chartrand 2012). We provide a general formulation containing both convex and non-convex functions because non-convex functions often showed better performance (Chartrand 2012, Kim et al. 2015a, Kim et al. 2015b). To guarantee convergence, we design an ADMM approach for TV combined with OS-SQS. Note that ADMM is a proximal splitting methods, which does not guarantee the global convergence when $\nu < 1$.

The majorizer of the cost function is

$$\hat{x} = \arg \min_x \phi_L^{(n)}(x) + \beta \left\| Rx \right\|_{h(\mu, \nu)}. \quad (7)$$

By setting a Lagrangian multiplier $\nu = Rx$, we can split variables using ADMM as follows (Goldstein & Osher 2009):

$$\min_{x, v, \eta} \phi_L^{(n)}(x) + \beta \|v\|_{h(\mu, v)} + \frac{\rho}{2} \|Rx - v - \eta\|_2^2, \quad (8)$$

where η is a dual variable, and $\mu = \beta/\rho$. Even though $\|v\|_{h(\mu, v)}$ is non-convex when $v < 1$, the cost function is strictly convex for the variable v . Eq. (8) can be solved by minimizing each variable alternatively:

$$x_j^{(n+1)} = \left[x_j^{(n)} - \frac{\frac{\partial \phi_{L,j}^{(n)}(x)}{\partial x_j} + \rho [R^H (Rx^{(n)} - v^{(n)} - \eta^{(n)})]_j}{d_{L,j}^{(n)} + \rho [R^H R]_j} \right]_+, \quad (9)$$

$$v_j^{(n+1)} = \text{shrink}_{\mu, \nu}(Rx_j^{(n+1)} - \eta_j^{(n)}), \quad (10)$$

$$\eta_j^{(n+1)} = \eta_j^{(n)} + (Rx_j^{(n+1)} - v_j^{(n+1)}), \quad (11)$$

where $[\]_+$ is the thresholding operator below zero, and the shrinkage operation (Chartrand 2012) is

$$\text{shrink}_{\mu, \nu}(l) = \max\{0, |l| - \mu |l|^{\nu-1}\} l / |l|. \quad (12)$$

Note that v and η have three directional components, and the shrinkage operation is calculated using each directional vector independently. R^H is the adjoint operator corresponding to R , which is the negative divergence (Chambolle 2004).

2.6. Setup

In our simulation study, we simulated exactly the same geometry of our prototype system, two detector and 40 rotational angles, as shown in figure 1. To evaluate the performance of detector sub-sampling, a high resolution phantom, shown in figure 4(a1), was used. Specifically, four configurations are used (radius/center to center distance, μm): (i) 200, (ii) 150/720, (iii) 80/280 and (iiii) 60/210. Monte Carlo (MC) simulations were conducted to explore the performance of maximum resolution for different methods. More specifically, emission events in object are randomly generated and then randomly detected in 8-DOI detector layers. Here, energy window, detector pair efficiency, scatter and random events were not considered in our simulation.

For quantification, the normalized root-mean-square error (NRMSEs, $\frac{\sqrt{\sum_j (x_j^* - x_j)^2}}{\sqrt{\sum_j (x_j^*)^2}}$) and bias

$(\frac{\sum_j |x_j^* - x_j|}{\sqrt{\sum_j (x_j^*)^2}})$ were calculated, where x^* and x denote the ground truth and reconstructed images, respectively. We also measure the ROI-based structural similarity (SSIM) index for comparing image quality. The SSIM is defined as $\frac{(2\mu_{r^*}\mu_r + c_1)(2\sigma_{r^*r} + c_2)}{(\mu_{r^*}^2 + \mu_r^2 + c_1)(\sigma_{r^*}^2 + \sigma_r^2 + c_2)}$, where r^* and r denote the ROIs of the ground truth and the reconstructed image, respectively. μ is the average, σ^2 is the variance and σ_{r^*r} is the covariance of intensity within the ROIs r^* and r . $c_1 = 2.5 \times 10^{-3}$ and $c_2 = 2.25 \times 10^{-2}$ were used. The full width at half maximum (FWHM) of the PSF was optimized using the minimum NRMSE. We consider a spatially invariant PSF with an FWHM of 225 μm .

We performed a point source experiment using a 10 μCi Na-22 point source (half life = 2.6 years) with a 250 μm diameter (Groll et al. 2017). Note that although ideally a point source should be smaller than a virtual detector pixel size, this phantom is one of the smallest commercially available point source phantoms. In our experiment, the point source was rotated to 40 angular positions with an offset of 1.304 mm from the center, where data for each position was acquired for an hour. By controlling the angular shift, we can add multiple point source datasets at other positions. To validate the resolution performance, we also controlled the distances between the sources manually. We used four point sources with distances from 380 μm to 630 μm as shown in figure 6(a). Sinograms without DOI, with rDOI and with sDOI were computed from the list-mode data. More specifically, a Michelogram with span 3 is used for axial compression with virtual detector, and 128 angular bins were used. The total measured photon counts were 16000. By discarding events, the reconstructed images for half and quarter doses are compared.

3. Results

3.1. Simulation

To demonstrate the robustness of the reconstructed image using the sDOI method, we compared the NRMSEs of the reconstructed images using OSEM without DOI, OSEM with rDOI and OSEM with sDOI for various rebinning resolutions in figure 3. Although OSEM without DOI and OSEM with rDOI showed worse NRSMEs for higher resolutions ($< 100 \mu\text{m}$), OSEM with sDOI provides stable NRMSEs for higher resolutions. We found that the optimal resolutions were different for methods without DOI, with rDOI and with sDOI. NRMSEs of sDOI does not change for higher than 50 μm rebinning resolution. Throughout this paper, the rebinning resolutions of 225 μm , 120 μm and 50 μm were used for reconstruction without DOI, with rDOI and with sDOI, respectively.

Figure 4 compares images reconstructed using OSEM, penalized OSEM with TV and ADMM-based TV for the without DOI, rDOI and sDOI cases. The PSF with FWHM of 22 μm was also applied selectively. The images in figures 4(a2)–(b4) were reconstructed using

OSEM with 6 iterations and 16 subsets. The images in figures 4 (c1)–(c4) were reconstructed using the proposed method with $\beta = 0.05$, $\rho = 0.002$, $\nu = 0.1$, 10 iterations and 16 subsets. We confirmed that the reconstructed images using sDOI and PSF were clearer at the sub-300 μm distance. In figure 5, the line profiles for OSEM using rDOI, penalized OSEM with TV using sDOI and ADMM-based TV using sDOI. All method applied the PSF with FWHM of 225 μm . The center distance between the two rods is 280 μm while the gap length is 200 μm . The line profiles with rDOI showed no distinction between the three rods, showed center bias (arrows in figure 5), and were generally very noisy. The line profiles with sDOI, on the other hand, did not show any center bias. The profile of penalized OSEM with TV using sDOI was sharper and noisier in flat regions. However, the ADMM-based TV using sDOI showed clear edges and was close to the ground truth. For the image quality comparison, table 1 compared SSIM, bias and NRMSEs of the penalized OSEM with TV and ADMM-based TV using rDOI and sDOI. Region (iii) in figure 4(a1) was used and the PSF with FWHM of 225 μm was applied. For all metrics, the ADMM-based TV using sDOI was the best.

3.2. Real experiment

In the phantom experiment, we compared images reconstructed by OSEM without DOI, OSEM using rDOI/PSF, OSEM using sDOI/PSF, penalized OSEM with TV using sDOI/PSF and ADMM-based TV using sDOI/PSF as shown in figure 6. The total photon counts were 16000, which can be considered sufficient for the point source study. The images in figures 6(b)–(e) were reconstructed using OSEM with 6 iterations and 16 subsets. The image in figures 6 (f) were reconstructed using the ADMM-based TV method with $\beta = 0.05$, $\rho = 0.002$, $\nu = 0.1$, 10 iterations and 16 subsets. In the reconstructed image without DOI in figure 6(b), the <300 μm apart point sources could not be distinguished. The images using OSEM with rDOI/PSF in figure 6(c) showed noisy and irregular structures despite PSF modeling. The image using OSEM with sDOI/PSF was clearer than that with rDOI/PSF. However this image showed some distortion and non-uniformity in the circular cross-section of the target. Penalized OSEM with TV using sDOI/PSF provided less distorted image as shown in figure 6(d). The reconstructed image of ADMM-based TV using sDOI/PSF retrieved a clearly circular target in figure 6(e) (see arrow).

Figure 7 compares line profiles of OSEM without DOI, OSEM using rDOI/PSF, penalized OSEM with TV using sDOI/PSF, and ADMM-based TV using sDOI/PSF. The minimum center distance between the two rods is 380 μm and the gap length is only 130 μm . Compared to penalized OSEM with TV, ADMM-based TV yielded a flatter (more uniform) profile at the center of the point sources. This is a confirmation of our claim that ADMM-based TV with sDOI and PSF is able to generate sub 300 μm resolution.

One of the key challenges in ultrahigh resolution PET imaging is the intrinsically low statistics. Figure 8 compares the reconstructed images for various total photon counts of 4000 (quarter), 8000 (half) and 16000. Reconstruction methods of OSEM using rDOI/PSF, OSEM using sDOI/PSF, penalized OSEM with TV using sDOI/PSF and ADMM-based TV using sDOI/PSF were compared. For higher dose, all methods using sDOI/PSF led to acceptable results. However, in the quarter-dose case, ADMM-based TV outperformed

penalized OSEM with TV. The reconstructed images using ADMM-based TV with sDOI and PSF exhibited lower noise levels and shape uniformity thereby indicating algorithm robustness for both quarter- and half-dose data.

4. Discussion

Our current work does not include positron range correction. Positron range correction is fundamentally important for our reconstruction since the intrinsic resolution of the system is comparable to the positron range of Na-22 as used in this study. Although we only use short positron range isotopes such as F-18 and Na-22 with approximately 200 and 260 μm full width at half maximum (FWHM) in water (Alessio et al. 2010), the blurring effect can significantly degrade the image quality in our system. Post-reconstruction Gaussian filtering can be simply used to compensate for the positron range artifacts (Bai et al. 2003). However, the positron migration depends on the object shape and materials. Thus, model-based positron range correction will be incorporated in our future work.

An accurate system modeling would require implementation of a spatially-variant PSF model into the iterative reconstruction framework. For accurate measurement of the PSF profile, a smaller point source ($\sim 50 \mu\text{m}$) should be used in subsequent experiments despite the limitations posed by detector sensitivity issues and insufficient tracer dose. Because the proposed method demonstrated the robust image quality visually even for quarter dose as shown in figure 8, the proposed method will be useful not only for a smaller point source but also for small animals with lower counts. Furthermore, axial sub-sampling based on virtual detectors was successfully implemented. However, we did not observe any clear benefits of this approach in our point source experiment. As future work, we seek to demonstrate that this approach not only leads to sub 300 μm radial resolution but also improves the axial accuracy of the proposed method by performing experiments using a miniature mouse brain phantom.

5. Conclusion

In this paper, we have introduced a data processing and reconstruction framework for a prototype ultrahigh resolution DOI-PET system. To reduce the computational complexity while taking advantage of the multi-layer DOI information, we proposed a high resolution virtual detector with uniform sub-sampling for efficient sinogram rebinning. To address elevated noise levels due to the lack of photon counts in the higher resolution bin, we proposed a penalized reconstruction technique using the Poisson log likelihood and a non-convex total variation penalty. Finally, the OS-SQS and ADMM algorithms were used to solve the resultant optimization problem. We demonstrated through a simulation study that the proposed sub-sampling method provides robust and higher resolution compared to sinograms without DOI and with rebinned DOI, and we found the optimal rebinning resolution was 50 μm for the sub-sampling method. Our preliminary point source study confirmed that reconstruction with the proposed method significantly improved the resolution of the system to sub-300 μm . We also demonstrated that the proposed reconstruction method yields a reduced noise variance, bias and SSIM, and more accurately restores the circular shape of the point source in the presence of low dose. As future work,

we will perform new experiments using a smaller point source, a spatially-variant PSF model, and a miniature mouse brain phantom to validate the sub 300 μm resolution for small animal imaging systems.

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Figure 1.

(a) A dual-detector coincidence setup and a compact CdTe detector developed for gamma ray imaging applications, and (b) a schematic illustrating the system with 8 depth-of-interaction (DOI). Here, $D = 34$ mm, $l = 22$ mm, and $d = 2$ mm.

Figure 2.

High-resolution virtual detector using (a) the rebinned DOI (rDOI) and the proposed sub-sampled DOI (sDOI) for (b) transaxial and (c) axial directions. Although the rebinning using rDOI can produce irregular and sparse bins as pointed in (i), the rebinning using sDOI can achieve more regular and robust sampling in high resolution space. w and d are the intrinsic resolutions of detector width and depth. u is a high resolution of virtual detector.

Figure 3.

NRMSE versus rebinning resolution using OSEM without DOI, rDOI and sDOI. OSEM reconstruction was performed with 6 iterations and 16 subsets. The rebinning resolutions of 225 μm , 120 μm and 50 μm were used for reconstruction without DOI, with rDOI and with sDOI, respectively.

Figure 4.

(a1) The ground truth, and images reconstructed using (a2) OSEM without DOI, (a3) OSEM with rDOI and (a4) OSEM with rDOI and PSF. Reconstructed images of (b) penalized OSEM with TV and (c) OS-SQS with ADMM-based TV using (1) rDOI, (2) rDOI with PSF, (3) sDOI and (4) sDOI with PSF. Four configurations were used (radius of rod / center to center distance, μm): (i) 200, (ii) 150/720, (iii) 80/280 and (iiii) 60/210. The red line in (a) is used for the line profile comparison in figure 5.

Figure 5. Line profiles for OSEM with rDOI, penalized OSEM with TV using sDOI and ADMM-based TV using sDOI. Three profiles used the PSF with FWHM of $225\ \mu\text{m}$. The red line in figure 4(a1) is used for the line profile comparison.

Figure 6.

(a) The configuration of the point sources, and the images reconstructed using (b) OSEM without DOI, (c) OSEM using rDOI/PSF, (d) OSEM using sDOI/PSF, (e) penalized OSEM with TV using sDOI/PSF, and (f) ADMM-based TV using sDOI/PSF. The red line in (a) is used for the line profile comparison in figure 7.

Figure 7.

Line profiles of OSEM without DOI, OSEM using rDOI/PSF, penalized OSEM with TV using sDOI/PSF, and ADMM-based TV using sDOI/PSF. The red line in 4(a) was used for the line profile.

Figure 8. Image comparison of (a) OSEM using rDOI/PSF, (b) OSEM using sDOI/PSF, (c) peanalized OSEM with TV using sDOI/PSF and (d) ADMM-based TV using sDOI/PSF for various total photon counts of (i) 4000, (ii) 8000 and (iii) 16000.

Table 1.

Comparison of SSIM, Bias and NRMSE of (a) penalized OSEM with TV using rDOI, (b) ADMM-based TV using rDOI, (c) penalized OSEM with TV using sDOI and (d) ADMM-based TV using sDOI. Region (iii) in figure 4(a1) was used for comparison, and all methods applied the PSF with FWHM of $225\ \mu\text{m}$.

	(a)	(b)	(c)	(d)
SSIM	0.11	0.16	0.21	0.38
Bias (%)	4.6	4.2	2.05	1.79
NRMSE (%)	5.01	4.64	2.46	2.18