Published in final edited form as:

IEEE Trans Nucl Sci. 2016 October ; 63(5): 2599–2606. doi:10.1109/TNS.2016.2607019.

Image-based Modeling of PSF Deformation with Application to Limited Angle PET Data

Samuel Matej [Senior Member, IEEE], Yusheng Li [Member, IEEE], Joseph Panetta [Member, IEEE], Joel S. Karp [Fellow, IEEE], and Suleman Surti [Senior Member, IEEE]

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

Samuel Matej: matej@mail.med.upenn.edu

Abstract

The point-spread-functions (PSFs) of reconstructed images can be deformed due to detector effects such as resolution blurring and parallax error, data acquisition geometry such as insufficient sampling or limited angular coverage in dual-panel PET systems, or reconstruction imperfections/simplifications. PSF deformation decreases quantitative accuracy and its spatial variation lowers consistency of lesion uptake measurement across the imaging field-of-view (FOV). This can be a significant problem with dual panel PET systems even when using TOF data and image reconstruction models of the detector and data acquisition process. To correct for the spatially variant reconstructed PSF distortions we propose to use an image-based resolution model (IRM) that includes such image PSF deformation effects. Originally the IRM was mostly used for approximating data resolution effects of standard PET systems with full angular coverage in a computationally efficient way, but recently it was also used to mitigate effects of simplified geometric projectors. Our work goes beyond this by including into the IRM reconstruction imperfections caused by combination of the limited angle, parallax errors, and any other (residual) deformation effects and testing it for challenging dual panel data with strongly asymmetric and variable PSF deformations.

We applied and tested these concepts using simulated data based on our design for a dedicated breast imaging geometry (B-PET) consisting of dual-panel, time-of-flight (TOF) detectors. We compared two image-based resolution models; i) a simple spatially invariant approximation to PSF deformation, which captures only the general PSF shape through an elongated 3D Gaussian function, and ii) a spatially variant model using a Gaussian mixture model (GMM) to more accurately capture the asymmetric PSF shape in images reconstructed from data acquired with the B-PET scanner geometry. Results demonstrate that while both IRMs decrease the overall uptake bias in the reconstructed image, the second one with the spatially variant and accurate PSF shape model is also able to ameliorate the spatially variant deformation effects to provide consistent uptake results independent of the lesion location within the FOV.

Index Terms

Reconstruction PSF deformation; limited angle data; parallax errors; image-based resolution modeling; TOF DIRECT reconstruction; histo-images; dedicated breast imaging; B-PET

I. Introduction

Dedicated breast PET scanners have a role to play not only in diagnostic imaging of patients with dense breast tissue where mammography has limited sensitivity [1], but also in tasks such as tumor characterization and monitoring response to therapy [2–4]. Quantitative, high-resolution PET images are needed to fully realize the benefits of dedicated PET imaging in these situations. Availability of a co-registered anatomical image is also desirable in order to better direct PET image guided biopsy, direct serial imaging of a localized region, and perform accurate attenuation correction of the PET image. One way of achieving these goals is to develop a combined breast PET-mammography or breast PET (B-PET)-digital breast tomosynthesis (DBT) system where the breast gets imaged in the same compressed position in a common gantry. A simple, and natural solution is the use of two flat panel PET detectors [5, 6] that are easily incorporated within the X-ray generator and detector setup of a DBT system (Fig. 1).

There are two potential drawbacks of such a design on the resultant PET image: increased parallax errors due to the small detector separation and consequently steep incident angles for annihilation photons with respect to the detector panel surfaces, and partial angular (limited angle) coverage due to the finite size of the detector panels; combination of both of those effects leads to significant point-spread-function (PSF) deformations in the reconstructed image and distortions in the direction orthogonal to the detector planes (as illustrated in Figs. 2-right and 3). The parallax error can, in principle, be decreased if the detector design allows the measurement of the depth-of-interaction (DOI) of the gamma-ray interaction within the detectors, but this typically entails other trade-offs in performance or in cost. On the other hand, the limited angular coverage of a non-TOF system violates Orlov's condition [7] and the consequent angular information loss cannot be recovered. We have shown, however, that TOF information can be utilized to reduce the consequence of angular information loss, and thereby reduce distortions and image artifacts and produce more quantitative images [5, 6].

In this work we combine the use of TOF image reconstruction with image-based resolution modeling (IRM) to capture PSF deformations related to reconstruction of limited angle data, parallax errors, as well as any other residual deformations, with the goal to decrease bias in lesion uptake measurement due to PSF deformations and especially to improve uniformity and consistency of small lesion uptake measurement throughout the imaging FOV. Although IRMs have been previously proposed and tested on traditional (cylindrical) PET systems, they have not been applied and studied for these kinds of data with such a strong anisotropic and asymmetric deformations. While the geometry we utilize is for two flat panel detectors in a dedicated breast imaging setup, the techniques will be applicable to other limited-angle PET scanner designs with other geometries. More generally, the presented methodology has much broader implications and is applicable to any PET system with deformed image PSF due to imperfect data corrections or image reconstruction.

II. Image-Based PSF modeling for B-PET Using DIRECT

A. Image-based PSF Deformation Modeling

Acquired emission data p for object/reconstructed image x are modeled in statistical iterative reconstruction algorithms as $p = \mathbf{A} x$, where $\mathbf{A}$ is the system matrix describing the emission and acquisition process. For more efficient reconstruction, the system matrix is often factorized into a sequence of operations modeling individual stages of this process [8, 9]:

$$\mathbf{A} = \mathbf{P}_{\text{Det. Sens}} \mathbf{P}_{\text{Det. Blur}} \mathbf{P}_{\text{Att}} \mathbf{P}_{\text{Geom}} \mathbf{P}_{\text{Img. Blur}}$$

where $\mathbf{P}_{\text{Det.Sens}}$ models detector sensitivity, $\mathbf{P}_{\text{Det.Blur}}$ models detector resolution (line-of-response, LOR) blurring, $\mathbf{P}_{\text{Att}}$ models attenuation, $\mathbf{P}_{\text{Geom}}$ is forward projection operation, and $\mathbf{P}_{\text{Img.Blur}}$ models image-based resolution effects, such as positron range or other resolution effects defined in object space. While accurate modeling of the data acquisition process provides an improvement in the lesion uptake measurement and uniformity for a complete angular coverage data set, for limited-angle coverage, or for imperfect or simplified reconstruction approaches, the reconstructed image may still be distorted in a spatially variant way, negatively affecting the quantitative interpretation of the image. TOF reconstruction helps to reduce the limited angle effects, but the timing resolution that is achievable in practice (e.g., 300 ps) is not adequate to fully eliminate these distortions. Here we propose to include in the IRM any reconstruction or resolution related PSF deformations and other residual effects not captured in the other modeling steps due to model imperfections or simplifications. Originally the IRM was used mostly for approximating data resolution effects in a computationally efficient way [10–17], but recently it was also used to mitigate effects of imperfect/simplified geometric projectors, such as Siddon or other simple ones [18, 19]. Our work goes beyond these applications by including in the IRM also PSF deformations present in images reconstructed from the limited angle data of dual panel PET systems.

In the dual panel B-PET scanner the reconstructed PSFs are strongly elongated in the direction orthogonal to the detector panels (see Fig. 3); compared to ~1.6-mm FWHM spatial resolution in-planes parallel to detectors, the orthogonal elongation is as much as 4-times this value. While the general PSF widths (FWHMs) have been found to be similar throughout the field of view, the PSF shape becomes highly asymmetric for locations out of the central plane from the mid-point between the detector panels (see Fig. 5b). In this work we obtained PSF deformation models for individual locations in the (FOV) by fitting the reconstructed point sources at those locations based on a Gaussian mixture model (GMM) using two (shifted) 3D Gaussians (see Section III.B). This model provided a good fit for the data from the studied B-PET system, but other models can be easily applied too.

In practical use, the resolution model can be obtained from point-source data acquisition [20–22] and their reconstruction for a sufficient set of representative locations to characterize the PSF shape and its changes throughout the reconstruction FOV. The PSF at each image voxel can then be obtained by interpolating the fitted PSF parameters (or alternatively of the PSF kernel values) from those obtained at the acquired point-source

locations [12–15]. In the dual panel system (in which the deformation can be well characterized by deformations in x, y, and z directions) the fitting/interpolations of the (GMM) kernel parameters can easily be done in the tri-directional way along x, y, and z-axes. In other systems, such as the ring PET systems with rotational symmetries, other parameterization and interpolation modes (based on rotational/spherical coordinates [12–15]) would be more appropriate.

B. DIRECT Reconstruction of Limited angle B-PET Data

Image-based resolution/deformation models are applicable to any non-TOF or TOF iterative reconstruction approach using list-mode, histo-projection or histo-image [23, 24] data, and using any reconstruction algorithm. In this work we have adapted Direct Image Reconstruction for TOF (DIRECT) approach to the dual panel data geometry.

The DIRECT approach is based on image-like partitioning of the data, which involves two steps: the acquired events are (1) sorted into a limited set of “views” according to the TOF angular sampling requirements and (2) histogrammed into a set of “histo-images” (one histo-image per view). Traditionally, binned TOF events are histogrammed into “histo-projections” (projections extended in the TOF direction). In the DIRECT approach, the acquired events are histogrammed directly into the “most-likely” voxels of the histo-images. Histo-images are defined by the geometry and desired sampling (voxel size) of the reconstructed image. Both acquired events and correction factors are placed into the voxels of their respective histo-images, which have a one-to-one correspondence with the reconstructed image voxels. Data and image with the same structure allow very efficient implementation of reconstruction and data correction operations.

Detector related resolution effects can be easily and efficiently applied within DIRECT forward- (FP) and back-projection (BP) operations [23, 25, 26]. Image-based resolution and PSF deformation modeling (IRM) operations (or their transpose) are applied in image space before and after FP and BP operations, respectively. In this work we combined all resolution effects into IRM, although some of them (such as parallax effects) could be modeled as part of the detector model within the FP and BP operations. For the IRM we implemented asymmetric and anisotropic kernels using fits based on the Gaussian mixture model (GMM). In the IRM tests and studies reported here we performed separate reconstruction for each evaluated lesion location using proper kernel for that location. The IRM operations using the spatially invariant kernels are very efficiently implemented in the Fourier domain as part of the DIRECT FP and BP operations. The spatially variant IRM tool will use spatial-domain 3D convolution-like operation. It can be implemented by applying a specific (interpolated) IRM kernel (or its transpose in the back-projection) at each voxel location. For practical kernel sizes this operation, even if performed in the spatial domain, is still faster than the rest of the DIRECT reconstruction operations. Furthermore, this operation can be easily and very efficiently implemented on a GPU, similar to our implementation of the spatially variant LOR models in [25].

In the DIRECT approach, the data are partitioned and processed view by view. Limited angular coverage of the dual panel B-PET system means that there is a range of the views that are completely missing. In addition, many of the available views are also not complete,

thus creating missing regions in the corresponding histo-images. This effect is modeled in DIRECT by utilizing the normalization histo-images generated by selectively depositing (histogramming) of the crystal-pair efficiency factors (only) along all valid LORs in the system into the histo-images. These normalization histo-images properly reflect crystal and geometric sensitivity in the histo-image regions with available data and contain missing (zero) histo-image regions where there are no available LORs (or views). This information is properly accounted for in the DIRECT projection, discrepancy and update operations.

III. Methods

A. Simulations

We performed Monte Carlo simulations in GATE [27] for the B-PET scanner geometry composed of two flat detectors as shown in Fig 2. These simulations assume a fixed geometry and detector dimensions that are comparable to the developed B-PET system (see Fig. 1), although in practice the detectors can be moved closer as the breast is put under mild compression. Each detector is composed of $1.5 \times 1.5 \times 15 \text{ mm}^3$ LSO crystals with system timing resolution of 300ps. No object scatter or random events were included in this simulation study focusing on the image-based PSF deformation effects.

For obtaining PSFs at (lesion) locations considered in our tests, we simulated a set of point sources in air located at 2-cm increments along three representative lines (in horizontal, vertical, and diagonal directions, as graphically represented in Fig. 2-left).

For the evaluation study, we simulated a breast phantom as a warm 14-cm diameter cylinder with uniform water attenuation containing a set of 25 5-mm diameter spheres with 4:1 and 8:1 activity:background ratios (shown in Fig. 2-right).

B. B-PET PSF Deformation Models

The PSF deformation models were obtained for individual locations in the (FOV) by fitting reconstructed point sources in air simulated at those locations. The PSFs were reconstructed without resolution modeling, and the reconstructions were run until convergence (i.e., until the PSF widths did not change). Ideally, these PSFs would be obtained from point sources in warm background that faithfully match the environment of each particular situation. However, it is challenging (and practically not feasible) to obtain accurate and reliable IRMs for statistical (non-linear) reconstructions based on point sources in warm background. The reconstructed PSF parameters and their convergence rates depend (spatially) on the particular object environment and characteristics, such as, local background levels, lesion/point-source contrast, object attenuation, counts, etc. Furthermore, convergence rates for the point sources in a warm background are considerably slower than in the air [28]. However, if we were to run the PSF reconstructions (for realistic background) for sufficient number of iterations to guarantee their uniform convergence throughout the FOV, the PSF shape parameter fits would become unreliable due to the increased noise, especially for realistic count levels. The main purpose of this work was to capture the general PSF deformation shape and its spatial variations in order to improve both the lesion quantitation and to make it spatially uniform throughout the FOV, and not necessarily to absolutely recover the PSF

deformations. Hence, we used point sources in air – a method that is also consistent with other works on IRM [12–16].

For the IRM to faithfully capture the shape (anisotropy, asymmetry, shifts, and PSF tails) of the spatially variant PSFs (RM-var) the IRM kernels were obtained for each point-source location by fitting the reconstructed PSFs with a GMM of two 3D Gaussian functions. The optimized parameters for each of the two 3D Gaussians were the widths (σ_x , σ_y , σ_z), shifts in x, y, and z directions, and their proportions (amplitude scales). The PSF fitting was performed using non-linear least-square fitting. Fig. 3 shows examples of the two fitting (3D) Gaussians, their GMM, and the corresponding y-profiles (in the elongated direction) for a PSF at $(x,y) = (0,6)$ cm which has a strong PSF deformation in the y-direction.

In the comparison studies, we also used a single spatially invariant (elongated) 3D Gaussian (RM-fixed) capturing just the general (average) PSF elongation and width, but not the asymmetry, mispositioning, and shape changes. For this purpose we used average of the 3D Gaussian fit parameters of the reconstructed PSFs over the FOV. We used fitting procedure as above, but fitted just a single 3D Gaussian with the fitting parameters being its widths (σ_x , σ_y , σ_z), and shifts in x, y, and z directions. Note that although we were fitting also the shift parameters for each location, their average gives zero overall shift for this system. Examples of the vertical profiles through the single Gaussian fit (blue line), double Gaussian GMM fit (red line), and reconstructed PSF (black line) at $(x,y) = (0,6)$ cm are shown in Fig. 4.

C. Phantom study, image reconstruction, and analysis

Reconstructions were performed using RAMLA algorithm [29, 30] within the DIRECT framework for both the PSF estimation as well as RM evaluation. We used 1-mm voxels, relaxation parameter 0.1, and performed a sufficient number of iterations to guarantee convergence of the PSF fits and CRC measures. In our studies we limited in the reconstructions the angular range to 17 transverse views (with angular steps 4.5° within $\pm 38^\circ$) and 11 axial views (with angular steps 6° within $\pm 33^\circ$). We compared 3 reconstructions; i) without resolution modeling (no RM), ii) with a simple fixed resolution model (utilizing spatially invariant single elongated 3D Gaussian; RM-fixed), and iii) using the GMM model using two 3D Gaussians fitted to a particular PSF obtained for each lesion location (RM-var).

Lesion uptake was measured by placing 5-mm diameter VOIs over each lesion location. Background uptake was measured as the average over multiple 5-mm diameter VOIs placed at matched transverse locations but in off-center slices (without lesions). Lesion contrast recovery coefficient (CRC) [31] was then calculated and used to estimate the quantitative accuracy. The variability in lesion CRC value due to location in FOV was measured by calculating the standard deviation of the CRC values across all lesion locations (including both spatial variations and noise effects on the CRC estimates).

IV. Results

A. Point source reconstructions – IRM generation and testing

Figs. 5a) and b) illustrate x- and y-profiles, respectively, through the reconstructed PSFs (star symbols) and their GMM fits (solid lines) at 9 representative locations of point source positioned along (top) x-axis, (middle) y-axis, and (bottom) a diagonal. Each individual plot is centered on the (simulated) location of the corresponding point source. PSF profiles in axial direction (z-profiles) were similar to the x-profiles. Comparisons of the x- and y-profiles demonstrate strong anisotropy of the PSFs in the form of elongation in the direction normal to the detector panels relative to the intrinsic spatial resolution $\text{FWHM}_x = 1.6 \text{ mm}$. Furthermore, while the general widths for individual directions are similar throughout the FOV, the PSF shapes are strongly asymmetric in the vertical (y) direction as one moves from $y=0\text{cm}$ to $y=6\text{cm}$ (see also Fig. 3), which is properly taken into account in the IRM by using the Gaussian mixture model for the distorted PSFs.

Fig. 6 demonstrates the convergence properties of the PSF reconstructions with and without IRM for point sources at two off-center locations near the horizontal ($x=6\text{cm}$, $y=0\text{cm}$) and vertical ($x=0\text{cm}$, $y=6\text{cm}$) edges of the reconstruction FOV. We compare the relative widths (FWHMs) of the reconstructed PSFs in the x and y directions; although the FWHM is only a very simple proxy of the PSF (non-Gaussian) shape in the y direction for the off-center locations along the y-axis, it adequately captures the general PSF width and convergence performance of the tested reconstructions. The point source data in air were reconstructed using three different reconstruction methods; i) no RM, ii) RM-fixed, and iii) RM-var. In the central plane ($y=0\text{cm}$) with the symmetric PSF shapes, even a single 3D Gaussian model is sufficient to capture the overall impact of the PSF deformation and both RM reconstructions converge to a single voxel (i.e., $\text{FWHM} = 1 \text{ mm}$). However, their convergence is substantially slower in the y direction of the PSF elongation compared to the noRM case. For the out-of-the-center plane ($y=6\text{cm}$) position, both RM reconstructions still converge to a single voxel in the x direction for which the PSF is symmetrical. On the other hand, only the RM-var (with accurate IRM model) converges to a single voxel in the y direction with an asymmetric PSF deformation. The convergence rates are further slowed down for the more complicated (asymmetric) PSFs, as occurs for $y=6\text{cm}$, as compared to the results for the symmetric PSFs, as occurs at $y=0\text{cm}$.

For simulated point sources (with a sub-voxel size) any statistical reconstruction from complete data and using accurate data models should converge to a single voxel (whether in air or a warm background). The purpose of this study was to test if the same is true also for the limited angle data (and with strong parallax effects) when using proper IRM reconstructions and to explore their convergence performance. Effects of the IRM on a practical, clinically more realistic, tasks and objects were subject of the breast lesion studies reported below.

B. Lesion phantom – IRM reconstruction evaluation

Fig 7 displays examples of reconstructions of the lesion phantom with (from left to right) no RM, RM-fixed, and a (single) RM-var reconstruction (using IRM kernel determined for the

location $x=0\text{cm}$, $y=6\text{cm}$). Note that for the RM-var evaluations in this study we used separate reconstructions for each lesion location with proper IRM kernel for that particular location. Future clinical RM-var implementation will involve spatially variant IRM operation, thus requiring only a single reconstruction for the whole FOV. The top row shows images from early iterations that are less noisy while the bottom row shows images from higher iterations at which the CRC measures in the individual reconstructions converged. In addition to the obvious increase in lesion contrasts with IRM, it is evident that the accurate IRM (RM-var) provides more spherical lesion shape. On the other hand, a consequence of the anisotropic resolution models (in both of the IRM cases) is the introduction of an anisotropic noise structures into the images with increased correlations in the direction of the PSF model elongation. The anisotropic correlations might have an impact on the detectability related diagnostic measures, however they do not impact the CRC measures assessing quantitative accuracy of the lesion uptake estimation evaluated in this work.

Figs. 8 and 9 show CRC measures for lesions at representative radial locations throughout the simulated B-PET FOV and for TOF reconstructions with different resolution models (no RM, RM-fixed, RM-var). The CRC values for each reported location are averages of 4:1 and 8:1 contrast lesions located at symmetrical positions (and having the same PSF shape). For lesions on x- and y-axis pairs of symmetrical 4:1 and 8:1 contrast lesions are averaged; for diagonal lesions four symmetrical CRC values (two for lesions with 4:1 contrast and two for lesion with 8:1 contrast) are averaged.

Fig 8 illustrates the CRC convergence properties for individual reconstruction models for lesions on the y-axis ($x=0\text{cm}$) with highly variable and asymmetric PSFs shapes. It can be seen that the IRM reconstructions converge to a higher CRC values, but at a considerably slower pace, compared to the reconstruction with no RM. However, only the accurate IRM reconstruction (RM-var) converges to uniform CRC values over the different lesion radial locations. In comparison, the RM-fixed reconstruction, which properly models only the PSF width but not its shape, gets saturated at lower, and less uniform, CRC values for the locations with the asymmetric PSF shapes.

Fig. 9 shows the converged CRC measures (at 40, 100, and 100 iterations for no RM, RM-fixed, and RM-var reconstructions, respectively) for lesions at all representative locations (on x-axis, y-axis, and diagonal) throughout the simulated B-PET FOV; confirming the convergence of the RM-var reconstructions to similar CRC values throughout the FOV.

Combined measures assessing overall CRC levels over all 25 lesions in the FOV (average CRC) and variability of the CRC values (standard deviation of CRC) and their trade-offs as functions of the iteration numbers for each of the three reconstructions are shown in Fig. 10, while their values at the final iterations (converged) are summarized in Table 1. It can be seen in the plots that the no-RM case saturates at low CRC value relatively quickly and further iterations just increase the CRC variability. While in the RM-fixed reconstruction the variability initially decreases as the mean CRC improves, it eventually (at about 30 iterations) starts to increase as the average CRC gradually saturates. On the other hand in the RM-var reconstruction the CRC variability substantially decreases as the reconstruction

converges (to the highest CRC values), while consistently providing the best CRC vs. variability trade-offs.

In summary, it can be seen from the plots and table that the IRM with the more accurate model of the PSF deformations (RM-var) is able to both improve the average CRC values (and decrease bias) and substantially decrease their variability throughout the FOV. In comparison, RM-fixed which only models the overall (elongated) PSF widths in x, y, and z directions but not the asymmetric shape and spatial variation within the FOV, also leads to higher average values of CRC, albeit with more variability throughout the FOV.

V. Discussion and Conclusions

Our results demonstrate the ability of properly designed IRMs to decrease the effects of the strongly asymmetric PSF deformations of the dual-panel B-PET system with limited angular coverage. Furthermore, spatially variant IRM faithfully capturing PSF at each lesion location throughout the FOV was shown to make the quantitative accuracy more robust independent of the location within the scanner field-of-view. Although the spatially variant IRMs have been studied before for traditional PET systems, none of the previous works involved a system with such strong asymmetries, anisotropies, and spatial variations that are characteristic of the dual panel PET system considered in this work. In this feasibility study we used separate reconstructions for each lesion location with its proper PSF model for that location for ease of implementation. Based on these promising results we will next implement a spatially variant IRM in our reconstruction algorithm, thereby varying the image-based resolution kernel within a single reconstruction. The IRM model will be determined from a limited set of representative PSFs at various locations, which will be interpolated in 3D to characterize the PSF at each image voxel. This will be followed by a quantitative evaluation of the IRM using realistic phantoms with lesions at various locations and local backgrounds.

In our studies, we modeled the PSF deformations using a Gaussian mixture model involving two (elongated and shifted) 3D Gaussians. This model provided a good fit of the shape of the PSFs obtained for the B-PET system, as demonstrated with simulated data generated with GATE and based on the geometry of this system; nevertheless, other models are easily applicable too. The PSF deformation model was based on converged reconstructions (without RM) of point sources in air. Although the PSFs for air might not exactly match (in absolute terms) the reconstructed PSFs in warm background, they provide robust estimates of general PSF shape and its changes throughout the FOV and were shown to lead to consistent lesion quantifications. In any case, even though obtaining of the reliable PSF estimates for exactly matched (non-zero) background environment might not be feasible, it is possible that adding a generic (ideal, uniform, low level, and no noise) background to the point source data (such as in [28]) might provide perhaps even more accurate PSF estimates.

The relatively wide, anisotropic, and asymmetric (for off-center locations) IRM kernels used for the limited angle data from the dual panel PET system result in slower, and spatially variable convergence properties, as compared to the case with no RM. In our studies, we evaluated the IRM results using 100 (RAMLA) iterations to be sure that the lesion CRC

measures were converged. Although it is not known yet if such a high number of iterations will be needed for practical applications, it is clear that a relatively high number of iterations will be needed for the dual panel PET system to guarantee uniform convergence of quantitative measures over the reconstructed FOV. Nevertheless, efficiency of the DIRECT reconstruction framework makes this goal clinically practical. On the other hand, when running reconstructions for many iterations, one will have to be also careful not to boost up the image noise levels too much, perhaps by applying proper post-smoothing or regularization.

Another side effect of the anisotropic IRM kernels is that they introduce anisotropic noise correlations into the reconstructed images. These do not affect estimation of the lesion uptake values, which was a main focus of this work. On the other hand, the anisotropic noise correlations might affect other clinical evaluation tasks, such as lesion detectability, and have to be properly taken into account when designing studies for such applications. For future work we will implement spatially variant IRM tools and perform detailed investigations of the IRM and reconstruction tools with simulated and experimental data acquired on the B-PET system that is under development and with applications relevant to its clinical use.

Acknowledgments

This work was partially supported by the National Institutes of Health under Grants R01-EB002131, R01-CA113941, R01-EB009056, and R01-CA196528. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Authors thankfully recognize Eunsin Lee for performing GATE simulations of the lesion phantom data, Matt E. Werner for helping with the generation of normalization and correction data, and Margaret E. Daube-Witherspoon and Scott D. Metzler for their valuable comments and suggestions on this work. We also thankfully acknowledge useful comments and suggestions from the associate editor and the anonymous reviewers of this paper.

References

1. Cole EB, Pisano ED, Kistner EO, Muller KE, Brown ME, Feig SA, et al. Diagnostic accuracy of digital mammography in patients with dense breasts who underwent problem-solving mammography: Effects of image processing and lesion type 1. *Radiol.* 2003; 226:153–160.
2. Dehdashti F, Mortimer JE, Trinkaus K, Naughton MJ, Ellis M, Katzenellenbogen JA, et al. PET-based estradiol challenge as a predictive biomarker of response to endocrine therapy in women with estrogen-receptor-positive breast cancer. *Breast Cancer Res Treat.* 2009; 113:509–517. [PubMed: 18327670]
3. Kurland BF, Gadi VK, Specht JM, Allison KH, Livingston RB, Rodler ET, et al. Feasibility study of FDG PET as an indicator of early response to aromatase inhibitors and trastuzumab in a heterogeneous group of breast cancer patients. *EJNMMI research.* 2012; 2:1–9. [PubMed: 22251281]
4. Eary, J.; Link, JM.; Mankoff, DA.; Muzi, M.; O'Sullivan, F.; Fink, J., et al. Novel PET imaging in the clinic: Selecting patient cohorts and measuring early response. *Proc. Am. Assoc. Cancer Res;* Chicago, IL. 2012 Mar 31–Apr 4;
5. Surti S, Karp JS. Design considerations for a limited angle, dedicated breast, TOF PET scanner. *Phys Med Biol.* Jun 7.2008 53:2911–2921. [PubMed: 18460745]
6. Lee E, Werner ME, Karp JS, Surti S. Design optimization of a time-of-flight, breast PET scanner. *IEEE Trans Nucl Sci.* Jun.2013 60:1645–1652. [PubMed: 24078744]
7. Orlov SS. Theory of three-dimensional reconstruction. 1. Conditions for a complete set of projections. *Soviet Physics Crystallography.* 1975; 20:312–314.

8. Qi J, Leahy RM, Hsu C, Farquhar TH, Cherry SR. Fully 3D Bayesian image reconstruction for the ECAT EXACT HR+ IEEE Trans Nucl Sci. 1998; 45:1096–1103.
9. Leahy RM, Qi J. Statistical approaches in quantitative positron emission tomography. Statistics and Computing. 2000; 10:147–165.
10. Reader AJ, Julyan PJ, Williams H, Hastings DL, Zweit J. EM algorithm system modeling by image-space techniques for PET reconstruction. IEEE Trans Nucl Sci. Oct.2003 50:1392–1397.
11. Rahmim A, Tang J, Lodge MA, Lashkari S, Ay MR, Lautamaki R, et al. Analytic system matrix resolution modeling in PET: An application to Rb-82 cardiac imaging. Phys Med Biol. Nov 7.2008 53:5947–5965. [PubMed: 18836219]
12. Cloquet C, Sureau FC, Defrise M, Van Simaey G, Trotta N, Goldman S. Non-Gaussian space-variant resolution modelling for list-mode reconstruction. Phys Med Biol. Sep 7.2010 55:5045–5066. [PubMed: 20702921]
13. Rapisarda E, Bettinardi V, Thielemans K, Gilardi MC. Image-based point spread function implementation in a fully 3D OSEM reconstruction algorithm for PET. Phys Med Biol. Jul 21.2010 55:4131–4151. [PubMed: 20601780]
14. Kotasidis FA, Matthews JC, Angelis GI, Noonan PJ, Jackson A, Price P, et al. Single scan parameterization of space-variant point spread functions in image space via a printed array: The impact for two PET/CT scanners. Phys Med Biol. May 21.2011 56:2917–2942. [PubMed: 21490382]
15. Angelis GI, Kotasidis FA, Matthews JC, Markiewicz PJ, Lionheart WR, Reader AJ. Full field spatially-variant image-based resolution modelling reconstruction for the HRRT. Physica Medica-European Journal of Medical Physics. Mar.2015 31:137–145.
16. Sureau FC, Reader AJ, Comtat C, Leroy C, Ribeiro MJ, Buvat I, et al. Impact of image-space resolution modeling for studies with the High-Resolution Research Tomograph. J Nucl Med. Jun. 2008 49:1000–1008. [PubMed: 18511844]
17. Stute S, Comtat C. Practical considerations for image-based PSF and blobs reconstruction in PET. Phys Med Biol. Jun 7.2013 58:3849–3870. [PubMed: 23681172]
18. Zhou J, Qi J. Efficient fully 3D list-mode TOF PET image reconstruction using a factorized system matrix with an image domain resolution model. Phys Med Biol. Feb 7.2014 59:541–559. [PubMed: 24434568]
19. Zhou, J.; Ye, H.; Balakrishnan, K.; Wang, W.; Qi, J. A hybrid image-space resolution model for fully 3D listmode reconstruction of TOF PET data. 2012 IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC); IEEE; 2012.
20. Alessio AM, Stearns CW, Tong S, Ross SG, Kohlmyer S, Ganin A, et al. Application and evaluation of a measured spatially variant system model for PET image reconstruction. IEEE Trans Med Imaging. Mar.2010 29:938–949. [PubMed: 20199927]
21. Panin VY, Kehren F, Michel C, Casey M. Fully 3-D PET reconstruction with system matrix derived from point source measurements. IEEE Trans Med Imaging. Jul.2006 25:907–921. [PubMed: 16827491]
22. Wiant D, Gersh JA, Bennett M, Bourland JD. Evaluation of the spatial dependence of the point spread function in 2D PET image reconstruction using LOR-OSEM. Med Phys. Mar.2010 37:1169–1182. [PubMed: 20384254]
23. Matej S, Surti S, Jayanthi S, Daube-Witherspoon ME, Lewitt RM, Karp JS. Efficient 3-D TOF PET reconstruction using view-grouped histo-images: DIRECT - Direct Image Reconstruction for TOF. IEEE Trans Med Imaging. May.2009 28:739–751. [PubMed: 19150784]
24. Daube-Witherspoon ME, Matej S, Werner ME, Surti S, Karp JS. Comparison of list-mode and DIRECT approaches for time-of-flight PET reconstruction. IEEE Trans Med Imaging. Jul.2012 31:1461–1471. [PubMed: 22410326]
25. Ha S, Matej S, Ispiryan M, Mueller K. GPU-accelerated forward and back-projection with spatially varying kernels in 3D DIRECT TOF PET reconstruction. IEEE Trans Nucl Sci. Feb.2013 60:166–173. [PubMed: 23531763]
26. Matej S, Daube-Witherspoon ME, Karp JS. Analytic TOF PET reconstruction algorithm within DIRECT data partitioning framework. Phys Med Biol. May.2016 61:3365–3386. [PubMed: 27032968]

27. Jan S, Santin G, Strul D, Staelens S, Assie K, Autret D, et al. GATE: a simulation toolkit for PET and SPECT. *Phys Med Biol.* 2004; 49:4543–4561. [PubMed: 15552416]
28. Ispiryan, M.; Matej, S. Image resolution effects in maximum-likelihood TOF PET reconstruction: Study of reconstruction and object influences. 2012 IEEE Nuclear Science Symposium and Medical Imaging Conference. Conference Record, CDROM, M10-35; Anaheim, CA. 2012;
29. De Pierro AR. On some nonlinear iterative relaxation methods in remote sensing. *Matematica Aplicada e Computacional.* 1989; 8:153–166.
30. Browne JA, De Pierro AR. A row-action alternative to the EM algorithm for maximizing likelihoods in emission tomography. *IEEE Trans Med Imaging.* 1996; 15:687–699. [PubMed: 18215950]
31. NEMA. Performance Measurements of Positron Emission Tomographs. Rosslyn, VA: National Electrical Manufacturers Association; NEMA Standards Publication NU 2 2008.

Fig. 1.

Diagram showing front view of the developed dual panel detector B-PET system with a breast located between the compression paddles with adjustable separation. This system is designed to be stationary and therefore results in limited angle coverage of the field-of-view.

Fig. 2.

Diagram of the simulated dual panel detector system with comparable angular range to the B-PET unit under development. The scanner axial FOV is 15-cm. **(Left)** Simulated point sources used for obtaining the parameters needed for the Image Resolution Model (IRM) were placed along x-axis, y-axis and diagonal directions consistently with the evaluated lesion locations (at 2, 4, and 6 cm radii). **(Right)** B-PET configuration with superimposed reconstructed image of the simulated lesion phantom. Phantom contains pairs (or double pairs for lesions on diagonals) of 5-mm lesions with 4:1 ($\phi = 45^\circ, 90^\circ, 180^\circ, 135^\circ$) and 8:1 ($\phi = 0^\circ, 135^\circ, 270^\circ, 315^\circ$) contrasts for symmetrical spatial locations (with matched IRMs).

Fig. 3.

Example of the Gaussian Mixture Model (GMM) fit for a PSF at extreme vertical position (at $y=6\text{cm}$). **Left:** central slices through the 1st and 2nd fitting 3D Gaussians and their mixture. **Right:** vertical profiles (in the elongation direction) through the fitting Gaussians and through the fitted reconstructed PSF (in black). Although we show only 2D slices/1D profiles in this example, the fitting was done in 3D.

Fig. 4.

Example of the vertical (y) profiles through the (blue line) RM-fixed IRM kernel using single representative 3D Gaussian, (red line) RM-var kernel using double 3D Gaussian within GMM fitted to each particular PSF location, and (black line) reconstructed PSF for the extreme out-of-the-center vertical position (at $y=6\text{cm}$).

Fig. 5.

Profiles ((a) x-profiles, (b) y-profiles) through the reconstructed point sources (star symbols) and PSF GMM fits (solid lines) for locations corresponding to lesion locations on (**top**) x-axis, (**middle**) y-axis, and (**bottom**) diagonals. Profiles are drawn through the exact locations at (x,y) cm (as labeled at the top left corner of each plot) of the simulated point sources (and not through the PSF maxima, which are shifted for the out-of-the-center locations for $y > 0$ cm). Horizontal axis labels are in millimeters and 0 in each plot is relative to the exact point source location.

Fig. 6.

FWHM (NEMA) measures (**left:** FWHM_x, **right:** FWHM_y, as functions of iterations) for point sources at two representative locations at the horizontal and vertical edges of the FOV for reconstructions using 3 IRM models (no RM, RM-fixed, RM-var). **Top:** point source in the central plane (at $x=6\text{cm}$, $y=0\text{cm}$), **bottom:** point source near the detector surface (at $x=0\text{cm}$, $y=6\text{cm}$).

Fig. 7.

Central slices of the lesion phantom reconstructed using: **left:** no RM, **middle:** RM-fixed, and **right:** RM-var (showing only a single reconstruction using IRM kernel for the particular location at $x=0\text{cm}$, $y=6\text{cm}$, highlighted by the red rectangle; for other locations separate RM-var reconstructions were performed with proper IRM for each location – not shown). Each image is scaled to its maximum to better show the reconstructed lesion shapes. Zoomed cut-outs below each image show the magnified region (red rectangle) around the bottom lesion (at $x=0\text{cm}$, $y=6\text{cm}$). Reconstructions are shown (**top**) for an intermediate number of iterations (10, 40, and 40, left to right, respectively) and (**bottom**) for a high (mostly converged) number of iterations (20, 100, and 100, left to right, respectively).

Fig. 8.

CRCs for individual lesion locations along the y-axis for reconstructions using variable number of iterations, demonstrating how the IRMs and their accuracy affect the CRC convergence properties.

Fig. 9.

CRCs for individual lesion locations (on x-axis, y-axis and diagonal, and at radial distances 2, 4, 6 cm from the center), each affected by a different level of the limited angle and DOI effects. Results are shown for converged CRC values in progression for reconstructions w/o RM (no RM), using representative simple spatially-invariant elongated 3D Gaussian (RM-fixed), and using IRM based on the PSF fits for each particular lesion location (RM-var).

Fig. 10.

CRC mean vs. variation (std of CRC) measures over all 25 individual lesions as a function of iterations (100 iterations shown with the increment of 10) for no RM, RM-fixed, and RM-var reconstructions; CRC variation was calculated as the standard deviation of the CRC in % of the CRC mean value at each given iteration).

TABLE I

Measures Over All 25 Individual Lesions

	No RM	RM-fixed (single Gauss)	RM-variable (double Gauss)
Average CRC	0.34	0.50	0.54
Std dev. CRC	14.1%	13.9%	7.6%