Fast direct estimation of the blood input function and myocardial time activity curve from dynamic SPECT projections via reduction in spatial and temporal dimensions

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(Received 17 January 2013; revised 11 July 2013; accepted for publication 12 July 2013; published 6 August 2013)

Purpose: Reconstruction of parametric images from dynamic single photon emission computed tomography (SPECT) data acquired with slow rotating cameras is a challenge because the estimation of the time–activity curves (TACs) may involve fitting data to an inconsistent underdetermined system of equations. This work presents a novel algorithm for the estimation of the blood input function and myocardial TAC with high accuracy and high efficiency directly from these projections.

Methods: In the proposed dynamic reconstruction method, the information from the segmentation of functional regions from the static reconstructed image was used as a prior to construct a sparse matrix, through which the spatial distribution of the radioactive tracer was represented. Then the temporal distribution of the radioactive tracer was modeled by nonuniform B-spline basis functions which were determined according to a new selection rule. With reduction in both the spatial and temporal dimensions of the reconstructed image, the blood input function and myocardial TAC were estimated using the 4D maximum likelihood expectation maximization algorithm. The method was validated using data from both digital phantom simulations and an experimental rat study.

Results: Compared with the conventional dynamic SPECT reconstruction method without the reduction in spatial dimensions, the proposed method provides more accurate TACs with less computation time in both phantom simulation studies and a rat experimental study.

Conclusions: The proposed method is promising in both providing more accurate time–activity curves and reducing the computation time, which makes it practical for small animal studies using clinical systems with slow rotating cameras. © 2013 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4816944>]

Key words: dynamic SPECT, slow-rotation, reduction in spatial and temporal dimensions, B-spline, ML-EM

1. INTRODUCTION

Single photon emission computed tomography (SPECT) is able to estimate the distribution of a radioactive tracer inside a patient based on a set of projections acquired sequentially as the camera rotates around the patient. In a conventional SPECT study, the tracer distribution is assumed to be temporally static during the acquisition, and transaxial images of the tracer distribution are reconstructed from acquired projections. This static SPECT study cannot quantify the temporal variation of biophysiologic or biochemi-

cal processes such as the perfusion or metabolism.¹ On the other hand, dynamic SPECT imaging is capable of tracking the radionuclide concentration changes over time with the assumption that the concentration is static during the time period of the data acquisition at each projection angle of the SPECT study, which has been reported to be widely utilized in different simulation,² preclinical,^{3,4} and clinical^{5–17} studies. The dynamic SPECT technique extracts the time–activity curves (TACs) of the radionuclide tracer in different tissues from a time series of reconstructed dynamic images and then estimates metabolic parameters through a

compartmental model¹⁸ or it extracts these parameters directly from projections.^{1,19} The TAC in the arterial plasma, called the blood input function, is crucial for the estimation of the parameters of the kinetic model.¹ The blood input function can be measured through blood sampling. However, this is invasive and impractical in some situations. Alternatively, researchers derive the blood input function from the reconstructed images in positron emission tomography (PET)^{20–22} and in SPECT with stationary detectors.²³ In SPECT systems with rotating cameras, due to the lower detection efficiency and the slow rotation of the camera, it is more difficult to derive the blood input function directly from the reconstructed images. This work develops a novel algorithm to estimate the blood input function and other organ tissue TACs directly from the projections accurately and efficiently.

In related work, many approaches have been developed to extract the TACs directly from SPECT projections. The “dSPECT method”^{24,25} fits the TACs for each voxel directly from projection measurements without any assumption about the location of the functional regions, and finds the peak activity from the result of two successive fits to the data. Humphries *et al.*²⁶ presented the “d²EM method” as a modification of the “dSPECT method” to improve the smoothness of the TACs with stronger constraints. Another approach is to apply factor analysis of dynamic structures (FADS), which extracts the TACs for a certain physiological region. Sitek *et al.*²⁷ used FADS to extract the TACs from the projections of the uptake and washout of ^{99m}Tc-MAG3 in kidneys. With high computational demand, the FADS approach took the functional region into consideration and included more constraints to guarantee the accuracy of the TAC.

In previously published works, the least-squares estimation of the spatiotemporal distribution from dynamically acquired SPECT was developed for TAC generation.¹ Especially, Reutter and his colleagues²⁸ developed an algorithm to utilize spatiotemporal basis functions to obtain the least-squares estimation of the TACs from dynamically acquired projection data. The TACs were an expansion of spatiotemporal basis functions where spatial basis functions obtained from the known anatomy were used to model the spatial distribution and predefined B-splines were used to model the temporal distribution of the radiopharmaceutical. This algorithm was then improved by utilizing spatial B-spline functions to model the spatial distribution²⁹ and applied in evaluation of the fatty acid metabolism in normal and spontaneously hypertensive rat hearts with ¹²³I-BMIPP.³⁰

In this study, we propose a new algorithm based on this previous work and develop refinements that are able to solve the difficult problem of estimating the time–activity curves in rodents with fast recirculation times (6–8 s) when acquiring the data with a slowly rotating SPECT camera (for instance, 90 s per rotation). The new algorithm estimates the TACs using prior spatial knowledge from the late static reconstruction to reduce the spatial dimensions of the reconstructed image, as well as quadratic B-splines to characterize the TACs with fewer parameters. These reductions in both spatial and temporal dimensions serve as the constraints in the estimation of the TACs, improve the accuracy of the estimation, and reduce the

computation time. The 4D maximum likelihood expectation maximum (ML-EM) algorithm is used in this paper to maximize a Poisson likelihood function instead of the least-square method in order to better represent the noise property in SPECT imaging. In addition, we introduce a static image segmentation procedure that designates two levels of uncertainty: segmentation with low and high confidence and incorporate the uncertainty into the iterative reconstruction procedure to reduce the influence of segmentation error on the accuracy of the TACs. We also develop a new rule to adaptively decide the distribution of knots for the B-splines instead of using predetermined knots.²⁸ This improves the accuracy of the TACs.

Both computer simulations and a rat study of ¹²³I-MIBG were used to illustrate the effectiveness and the stability of the proposed method. ¹²³I-MIBG, an analog of the norepinephrine uptake in the presynaptic portion of the sympathetic neurons that innervate the heart, was used to evaluate the change in neural activity in the heart of the Wistar-Kyoto (WKY) normal rat and a spontaneously hypertensive rat (SHR) with the progression of left ventricular hypertrophy. The difference between the uptake and washout of the tracer in WKY and SHR reflected the severity of cardiac hypertrophy.¹⁶ The method proposed in this paper combined with the SPECT imaging of ¹²³I-MIBG can be translated to the clinic for improved diagnosis and management of therapy for patients with heart failure.

2. METHOD

The proposed method segments the functional ROIs from the static reconstructed image to construct the spatial sparse matrix and the B-spline functions for modeling the temporal activity of the radiotracer. For the dynamic reconstruction, the 4D reconstructed image is spatially represented by the coefficients of the spatial sparse matrix and temporally represented by the coefficients of the B-spline basis functions. The proposed method is implemented in three steps: the reconstruction of the late 3D static image, the construction of a sparse matrix representing the spatial ROIs, and the reconstruction of the 4D dynamic spatial and temporal distributions.

2.A. Reconstruction of the late 3D static image

The late 3D static image is the reconstruction of projections after the tracer activity has stabilized in the myocardium and there is very little change in the distribution from one 360° tomographic acquisition to another. The late dynamically acquired projections are summed and a static image is reconstructed for the purpose of segmentation using the ML-EM.³¹ This algorithm is expressed as

$$\hat{x}_j^{n+1} = \frac{\hat{x}_j^n}{\sum_i f_{ij}} \sum_i f_{ij} \frac{p_i}{\sum_{j'} f_{ij'} \hat{x}_{j'}^n}, \quad (1)$$

where $\hat{x}_j^n$ is the activity estimated in voxel j , $j = 0, \dots, J - 1$ after n iterations, p_i is the projection data in projection bin i , $i = 0, \dots, I - 1$, and f_{ij} is the probability that the photon emitted from pixel j is detected in bin i . The summation over

j' denotes the operation of projection. The summation over i denotes the operation of backprojection.

2.B. Construction of the sparse matrix

The static reconstructed image reveals the location of radiotracer accumulated in different functional regions. By assuming that the radioactivity in each functional region of the image is distributed uniformly, the static reconstructed image can be segmented to different uniform regions. Correspondingly, the segmentation provides a binary matrix

$$\Psi_{J \times M} = \begin{Bmatrix} \psi_{11} & \cdots & \psi_{1M} \\ \vdots & \ddots & \vdots \\ \psi_{J1} & \cdots & \psi_{JM} \end{Bmatrix}, \quad (2)$$

where the entry in $\Psi_{J \times M}$ identifies whether a pixel in the image belongs to a specific region. For example, $\psi_{mj} = 1$ means the j th pixel exclusively belongs to the m th region, otherwise $\psi_{mj} = 0$. Hence, for an image with J pixels (J rows in $\Psi_{J \times M}$), $M - 1$ of the entries in the M columns (M regions) are zero.

With the sparse matrix $\Psi_{J \times M}$, the image to be reconstructed can be spatially represented by s_m , the coefficients of the sparse matrix

$$x_j = \sum_m \psi_{jm} s_m. \quad (3)$$

Since the low spatial resolution of the SPECT image makes it difficult to be segmented, the sparse matrix actually contains two submatrices

$$\Psi_{J \times M} = [\mathbf{R} | \mathbf{O}]. \quad (4)$$

The column vectors in $\mathbf{R}$ represent those functional regions segmented with a high degree of confidence, while the column vectors in $\mathbf{O}$ represent those remaining to be ambiguous, such as the distribution between different functional regions. We used the K-means algorithm to determine the membership of each voxel to these regions represented by the vectors in $\mathbf{R}$. If the voxel belongs to a certain region in $\mathbf{R}$, the corresponding element in $\mathbf{R}$ is set to be 1. If the voxel is uncertain to belong to a certain region in $\mathbf{R}$, it is then considered to be in a transitional area between different functional regions, which determines an element in $\mathbf{O}$ to be 1.

2.C. 4D dynamic reconstruction

The model for the projections for dynamic SPECT is denoted by

$$p_i(t) = \sum_j f_{ij} x_j(t), \quad (5)$$

where $p_i(t)$ is the projection data in the i th projection bin at time t , $t = 1, \dots, T$ (for this paper T is 90 s), and $x_j(t)$ is the activity in pixel j at time t .

With the sparse matrix $\Psi_{J \times M}$, the 4D reconstructed image is spatially represented as

$$x_j(t) = \sum_m \psi_{jm} s_m(t), \quad (6)$$

where $s_m(t)$ is the coefficients of the m th vector (m th region) in the sparse matrix $\Psi_{J \times M}$. The number of unknowns in the spatial dimensions is reduced from J (64×64 in this study, see Sec. 3.A) to M (6 in this study).

Even though the number of unknowns is reduced through the reduction in the spatial dimensions of the 4D image, reconstructing from dynamic SPECT data is more likely to be an underdetermined problem because of the acquisition of data from small animals with fast recirculation times (for instance, 6–8 s for rodents) using slow rotating cameras (for instance, 90 s per rotation). Fortunately, the continuity of the temporal variation can be used to minimize this problem. For instance, the B-spline functions are introduced to model the TACs of each region. With the B-spline basis functions [Fig. 1(a)], the $s_m(t)$ is represented temporally as

$$s_m(t) = \sum_k c_{mk} b_k(t), \quad (7)$$

where $b_k(t)$ is the value of the k th B-spline basis function at time t and c_{mk} is the coefficient of the k th B-spline basis function for the m th region. The number of unknowns in the temporal dimensions is reduced from T (90 in this study) to K (the number of the B-spline basis functions).

Combining (6) and (7), the 4D image to be reconstructed is written as

$$x_j(t) = \sum_m \sum_k \psi_{jm} c_{mk} b_k(t). \quad (8)$$

The model for the projections for dynamic SPECT after the reduction in both spatial and temporal dimensions is rewritten as

$$p_i(t) = \sum_j \sum_m \sum_k f_{ij} \psi_{jm} c_{mk} b_k(t). \quad (9)$$

With the assumption that the concentration is static during the acquisition at each angle, t is a discrete variable which can be written as

$$t = \left\lfloor \frac{i}{D} \right\rfloor, \quad (10)$$

where D is the number of detector bins (for this paper, it is 120×88), i is the index of the projection bins, and $\lfloor \cdot \rfloor$ is the floor function, which means the integer part of a real number.

During the 4D iterative reconstruction, the unknown parameter c_{mk} to be reconstructed is updated by the 4D ML-EM algorithm:

$$\begin{aligned} \hat{c}_{m,k}^{n+1} = & \frac{\hat{c}_{m,k}^n}{\sum_i \sum_j f_{ij} \psi_{jm} b_k(\lfloor i/D \rfloor)} \sum_i \sum_j \left\{ f_{ij} \psi_{jm} b_k(\lfloor i/D \rfloor) \right. \\ & \times \left. \frac{P_i(\lfloor i/D \rfloor)}{\sum_{j'} \sum_{m'} \sum_k f_{ij'} \psi_{jm'} \hat{c}_{m',k}^n b_k(\lfloor i/D \rfloor)} \right\} \end{aligned} \quad (11)$$

FIG. 1. (a) The uniform B-spline basis functions. (b) Selected knots in normalized curvature of TAC. (c) Nonuniform B-spline basis functions.

The time-activity curve of the m th functional area is obtained by

$$s_m(t) = \sum_{k=1}^K c_{m,k} b_k(t). \quad (12)$$

The choice of the B-spline basis functions $b_k(t)$ can affect the accuracy and efficiency of the estimation of the TACs.

Selecting too many basis functions increases the complexity and causes misinterpretation of the high frequency noise as temporal variations of the uptake and washout. At the same time, too few basis functions can influence the accuracy of the time-activity curve by inadequate modeling of the peak of the uptake. In this study we develop a new rule for choosing the B-spline basis functions. Initially, the knots of the B-spline basis functions are uniformly distributed [for instance, Fig. 1(a)], such that the number of B-spline basis functions is decided according to the prior knowledge of the study. After five iterations of the ML-EM reconstruction with the current B-splines, a new set of B-splines are updated automatically according to the following procedure:

Step 1: Obtain the normalized curvature of the blood pool TAC $s_{\text{blood}}(t)$ estimated with the current B-spline basis functions, as shown in Fig. 1(b). The curvature is defined as,

$$\text{Curvature}(t) = \frac{\left| \frac{d^2 s_{\text{blood}}(t)}{dt^2} \right|}{\left(1 + \left(\frac{ds_{\text{blood}}(t)}{dt} \right)^2 \right)^{3/2}}. \quad (13)$$

Step 2: Decide the knots from the blood pool TAC estimated with the current B-spline basis functions and its normalized curvature.

- (1) Choose the first and the last time points ($t = 0$ s and $t = 90$ s in this study) in the estimated TAC as the first and the last knots of the B-splines, respectively.
- (2) Choose the first time point with a nonzero activity in the estimated TAC as a knot.
- (3) Choose the local maximum points [points 1–5 in Fig. 1(b)] in the curvature of TAC within the early 30 s (based on our prior knowledge about the metabolism of ^{123}I -MIBG) as knots.
- (4) Choose the first point in the curvature of TAC within the last 30 s with a value lower than 0.01 [point 6 in Fig. 1(b)] as a knot.

The selected knots are located at 0, 1, 3, 8, 13, 18, 23, 36, and 90 s.

Step 3: Construct the new nonuniform B-spline basis functions based on the selected knots as shown in Fig. 1(c).

2.D. Metric for evaluation

To analyze the TACs estimated by different methods, we use the relative root mean square (rRMS) error²⁶ to evaluate the relative difference between the estimated TACs and true TACs. The relative root square error is calculated as,

$$\text{rRMS} = \frac{\| \text{TAC}^{\text{est}} - \text{TAC}^{\text{tr}} \|_2}{\| \text{TAC}^{\text{tr}} \|_2} \times 100\%, \quad (14)$$

where $\| \cdot \|_2$ is the l^2 norm, TAC^{est} is the vector representing the estimated TAC, and TAC^{tr} is the vector representing the true TAC for the same region as the estimated TAC.

3. SIMULATION STUDY

The proposed method was assessed through a simple phantom study and a 3D Mouse Whole-Body (MOBY) digital phantom³² study. In this section, the estimation of the TACs was compared between the proposed method with the reduction in both spatial and temporal dimensions and the 4D reconstruction with the same temporal processing without the reduction in spatial dimensions to evaluate the effectiveness of reduction in the spatial dimensions. A comparison between the proposed method and a different method²⁸ for selecting the distribution of the knots was also performed to certify that the proposed method does improve the accuracy of the estimated TACs. Additionally, the effect of the itera-

tion number and the noise on the accuracy of the TACs was assessed.

3.A. Phantom simulation

The performance of the proposed method was validated using a simple $64 \times 64 \times 64$ -voxel phantom with two spheres [Fig. 2(a)], denoted as A and B, and $64 \times 64 \times 64$ MOBY rat phantom [Figs. 2(b) and 2(c)] with the cardiac cycle set to be 0.2 s, similar to a real situation. The voxel size of the MOBY phantoms is $0.65 \times 0.65 \times 0.65$ mm³.

The dynamic activity was distributed in region A and region B in the sphere phantom, while in blood pool,

FIG. 2. The sphere phantom (a), the MOBY phantom at end-diastole (b) and end-systole (c), the simulated activity curves in sphere phantom (d), and the simulated activity curves in MOBY phantom (e).

myocardium and liver in MOBY phantom. In practice the acquisition is performed for 100 min to follow the washin and washout of ^{123}I -MIBG from the heart (see Sec. 4). The washout is an important indicator for prognosis of those with heart failure. In this study we were not concerned with the washout phase of the study but focused on developing methods that could estimate the early phase (for example, in the 90 s of the first rotation) of blood and myocardial tissue time–activity curves. This is the more difficult part of the problem but is essential before we can model the full kinetics of both the washin and washout. In this study, the dynamic activity for each region was generated over 90 s [Figs. 2(d) and 2(e)]. The time activities for each region after 90 s were assumed to be the same as that at the 90th second. The projection data from 90 s to 100 min were only utilized to reconstruct a static image such that functional regions could be segmented. However, in practice in order to estimate clinically useful rate parameters, real activities after 90 s (as was accumulated for the rat study in Sec. 4) will be obtained from corresponding projections.

The projections of two phantoms were simulated based on a dual-head GE Millennium VG3 Hawkeye SPECT/CT scanner with the detector heads arranged in H-mode and equipped with custom designed pinhole collimators of tungsten with rectangular apertures of 1.5×2 mm. The point response of the pinhole was simulated while no scatter or attenuation was

included. Each of the two heads acquired data at 90 angles each for 1 s to finish one rotation, making a 90×2 projection data set. Since the activity was assumed to vary during the data acquisition, the index of the angle determined the temporal information. The number of the detector bins was 120×88 hence the projections formed a volume of $120 \times 88 \times 180$ for each rotation. There were in total 66 rotations.

3.B. Evaluation of the reduction in spatial dimensions

The TACs of the two phantoms estimated with the proposed method and the 4D reconstruction with the same temporal processing but without the reduction in spatial dimensions are shown in Fig. 3. The method with the same temporal processing but without the reduction in spatial dimensions was processed as follows:

- (1) The activity in each voxel was estimated using only the temporal B-spline functions.
- (2) The time–activity curve of the region was calculated by averaging the time–activity curves over the voxels in the region.

For the sphere phantom, the rRMS error of the TACs of region A and region B estimated by the proposed method was 1.02% and 0.34%, while the method without the reduction in

FIG. 3. The estimated TACs of (a) region A and (b) region B for the sphere phantom, and the estimated TACs of the blood (c) and the myocardium (d) for the MOBY phantom by the proposed method and the method without the reduction in the spatial dimensions.

FIG. 4. The true TACs and the estimated TACs of the blood (a) and the myocardium (b) by the previous method in Ref. 28 for selecting the distribution of knots of the B-splines.

spatial dimensions was 33.06% and 6.34%. For the MOBY phantom, the rRMS error of TACs for the blood and the myocardium estimated by the proposed method was 5.79% and 1.47%. It was 39.07% and 20.22% for the method without the reduction in spatial dimensions. It is evident that the proposed method offers more accurate time–activity curves.

3.C. Evaluation of the method for selecting the distribution of knots

The selection of the distribution of knots of the B-spline basis functions in the temporal dimensions also has influence on the accuracy of the TACs. Figures 3(c) and 3(d) show the TACs of the blood pool and the myocardium for the MOBY phantom estimated using the method in this paper, while Figs. 4(a) and 4(b) show TACs estimated with the method presented in previous work,²⁸ where the knots of the B-splines were located at 0, 2.4, 9.4, 30, and 90 s. The rRMS error for the blood TAC estimated by our proposed method was 5.79%, which is similar to 5.61% by the previous method, while for the myocardium it was 1.47%, much smaller than 3.64% by the previous method. This suggests that our proposed method

for selecting the distribution of the knots may be more accurate.

3.D. Number of iterations and computational expenditure

The accuracy of the estimated TACs as a function of the number of iterations is shown in Fig. 5. The rRMS error (shown every five iterations) decreases with the increasing number of iterations. The computation stops when the reduction in rRMS in successive iterations is less than a pre-defined limit. At iteration 40, the rRMS only reduces by $2.5 \times 10^{-3}\%$ for the sphere phantom and $2.46 \times 10^{-2}\%$ for the MOBY phantom compared to that at iteration 35, indicating the steady state is reached. Reconstructions in this paper were all carried out with 40 iterations if not indicated explicitly.

The rRMS error of the TAC for the sphere phantom is obviously smaller than that for the MOBY phantom. This is because the heart in the MOBY phantom is in motion with the change of time, resulting in an error in the construction of the spatial sparse matrix.

FIG. 5. The rRMS error for the TACs estimated after each iteration in the study for (a) the Sphere phantom and (b) the MOBY phantom.

As for the MOBY phantom, the rRMS error of the blood TAC is greater than that of the myocardium TAC. One of the reasons for this phenomenon is that the curvature of the blood TAC is greater than that of the myocardium. It is more difficult to model the blood TAC than the myocardium TAC. In addition, errors in selecting parts of the myocardium as blood areas in constructing the spatial sparse matrix also contributes to this phenomenon. However, the effect of this is reduced by introducing transitional regions in the construction of the spatial sparse matrix. Moreover, the difference in the estimation error between ROIs can also result from the different spatial properties of the ROIs.

Since the reduction in the spatial and temporal dimensions of the image to be reconstructed greatly reduces the number of the unknowns, the computational problem with 4D dynamic reconstruction is better conditioned. The time required in the proposed method is 56 s, while the traditional method without reduction in the spatial dimensions is 5 h on the Intel(R) X5650 2.66 GHz, 48 GB workstation. That is to say, the time consumed by the proposed method is 300 times less than that by the method without reduction in the spatial dimensions, thus making the proposed method more practical for clinical applications.

3.E. Noise evaluation

To study the effects of noisy projections on the accuracy of TACs estimated with the proposed method, 100 realizations of projections with two levels of Poisson noise were generated for the MOBY phantom. The total counts of the $120 \times 88 \times 180$ projections for Noise Level 1 were 10^5 and 10^6 for Noise Level 2.

Figure 6 shows the average TACs of the 100 realizations of noise estimated for the blood pool and the myocardium. For both regions, the differences between the average of the estimated TACs and the true TACs are fairly small, which indicates the proposed method is accurate. The tight short error bars shown in Fig. 6 indicate that this method is stable. As described in this paper, the late dynamically acquired projections were summed and a static image was reconstructed for the purpose of segmentation. The summation operator smoothes the noise. For the 4D reconstruction, at each iteration all functional regions were assigned the same value since we assumed these regions were uniform, which averages the voxels in each region and thus smoothes the noise. Moreover, the fitting to splines also smoothed the data in time. The rRMS error of the TACs of the blood pool and the myocardium

FIG. 6. The average TAC of 100 realizations for the blood with Noise Level 1 (a), the myocardium with Noise Level 1 (b), blood with Noise Level 2 (c), and myocardium with Noise Level 2 (d). The error bars represent the standard deviation.

TABLE I. rRMS error of the time–activity curves for the blood pool and the myocardium (%).

	Without noise	Noise Level 1	Noise Level 2
Blood pool	5.79	8.84 ± 2.14	6.06 ± 0.72
Myocardium	1.47	3.17 ± 0.80	1.71 ± 0.30

estimated from different noisy projections is shown in Table I. The TACs estimated from more noisy projections (Noise Level 1) have larger rRMS error than those from the less noisy projections data (Noise Level 2). It is necessary to point out that Noise Level 2 more so than Noise Level 1 matches the real noise level in our rat study.

4. RAT STUDY

The data for the rat study were acquired with a dual-head GE Millennium VG3 Hawkeye SPECT/CT scanner with the detector heads arranged in H-mode and equipped with custom designed pinhole collimators of tungsten with rectangular apertures of 1.5×2 mm. In each study, approximately 5 mCi of ^{123}I -MIBG was injected into a tail vein of the rat simultaneously with the start of dynamic data acquisition. Data were acquired for 100 min with an angular step of 2° lasting for 1 s per angle.

The late data acquired 1.5–100 min after injection were summed and reconstructed. The 3D static reconstructed image is shown in Fig. 7(a). The estimated TACs of the blood pool and the myocardium with the two methods are shown in Figs. 7(b) and 7(c).

5. DISCUSSION AND CONCLUSION

In this work, a fast method for estimation of the blood input and the myocardial TACs from dynamic SPECT projections was proposed. The method reduced the number of unknowns in the 4D iterative reconstruction both for the spatial and the temporal variables to improve the conditioning of the problem and lower the computational cost. In the spatial domain, functional regions segmented from the static reconstructed image were used to construct a sparse matrix, through which the number of spatial unknowns of the 4D image to be reconstructed was reduced. For the temporal domain, B-spline functions were selected via a newly developed approach to better model the TACs of data acquired in rodents with fast recirculation times using slow rotating gamma cameras.

It is fair to point out that the proposed method reduces the number of unknowns while at the same time may introduce errors due to segmentation. Our current efforts and our eventual research goals are to minimize these errors and improve the estimation accuracy. As is shown in Fig. 3, the proposed method, compared to the method without the reduction in spatial dimensions, improved the accuracy of the blood input function for both the simple spherical phantom study and the more realistic MOBY phantom study. In our simulations we did find that in the MOBY phantom study the accu-

FIG. 7. The late 3D static image of the rat heart (a). The estimated TACs of the blood (a) and the myocardium (b) by the proposed method and the method without reduction in the spatial dimensions (averaged over voxels in the ROI) for the same rat data.

racy of the TACs was degraded by the segmentation error due to the heart motion. Nevertheless, the degradation was small [Figs. 3(c) and 3(d)] primarily due to the introduction of the transitional regions in the construction of the sparse matrix. We hypothesize that the result (Fig. 7) for the experimental rat data will have the same improved accuracy as we observed in the MOBY phantom simulation.

More studies will be performed to investigate if introducing the fuzzy clustering method³³ can further reduce the effect of segmentation error and further improve the accuracy of the TACs. Our future work will also include the simultaneous estimation of TACs and kinetic modeling pa-

parameter and the investigation on shortening acquisition times to make the algorithm more practical for clinical studies on condition that we can obtain meaningful rate parameters.

ACKNOWLEDGMENTS

This work is funded by the National Science Foundation of China (Nos. 81201114 and 81271610) and by NIH Grant Nos. R01 HL50663 and R01 EB07219 and by the Director, Office of Science, Office of Biological and Environmental Research of the US Department of Energy under contract DE-AC02-05CH11231.

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