Quantitative simultaneous $^{99m}\text{Tc}/^{123}\text{I}$ cardiac SPECT using MC-JOSEM

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(Received 8 September 2008; revised 11 December 2008; accepted for publication 12 December 2008;
published 27 January 2009)

Simultaneous rest ^{99m}Tc -Sestamibi/ ^{123}I -BMIPP cardiac SPECT imaging has the potential to replace current clinical ^{99m}Tc -Sestamibi rest/stress imaging and therefore has great potential in the case of patients with chest pain presenting to the emergency department. Separation of images of these two radionuclides is difficult, however, because their emission energies are close. The authors previously developed a fast Monte Carlo (MC)-based joint ordered-subset expectation maximization (JOSEM) iterative reconstruction algorithm (MC-JOSEM), which simultaneously compensates for scatter and cross talk as well as detector response within the reconstruction algorithm. In this work, the authors evaluated the performance of MC-JOSEM in a realistic population of $^{99m}\text{Tc}/^{123}\text{I}$ studies using cardiac phantom data on a Siemens e.cam system using a standard cardiac protocol. The authors also compared the performance of MC-JOSEM for estimation tasks to that of two other methods: standard OSEM using photopeak energy windows without scatter correction (NSC-OSEM) and standard OSEM using a Compton-scatter energy window for scatter correction (SC-OSEM). For each radionuclide the authors separately acquired high-count projections of radioactivity in the myocardium wall, liver, and soft tissue background compartments of a water-filled torso phantom, and they generated synthetic projections of various dual-radionuclide activity distributions. Images of different combinations of myocardium wall/background activity concentration ratios for each radionuclide were reconstructed by NSC-OSEM, SC-OSEM, and MC-JOSEM. For activity estimation in the myocardium wall, MC-JOSEM always produced the best relative bias and relative standard deviation compared with NSC-OSEM and SC-OSEM for all the activity combinations. On average, the relative biases after 100 iterations were 8.1% for ^{99m}Tc and 3.7% for ^{123}I with MC-JOSEM, 39.4% for ^{99m}Tc and 23.7% for ^{123}I with NSC-OSEM, and 20.9% for ^{99m}Tc with SC-OSEM. The relative standard deviations after 30 iterations were 0.7% for ^{99m}Tc and 1.0% for ^{123}I with MC-JOSEM, as compared to 1.1% for ^{99m}Tc and 1.2% for ^{123}I with NSC-OSEM and 1.3% for ^{99m}Tc with SC-OSEM. Finally, the authors compared the relative standard deviation after 30 iterations with the minimum theoretical variance on activity estimation, the Cramer–Rao lower bound (CRB), and with the biased CRB. The measured precision was larger than the biased bound values by factors of 2–4, suggesting that further improvement could be made to the method. © 2009 American Association of Physicists in Medicine. [DOI: [10.1118/1.3063544](https://doi.org/10.1118/1.3063544)]

Key words: iterative reconstruction, MC-JOSEM, cardiac SPECT, dual-radionuclide

I. INTRODUCTION

Simultaneous ^{99m}Tc -Sestamibi/ ^{123}I -BMIPP cardiac SPECT imaging has the potential to replace the current clinically implemented ^{99m}Tc -Sestamibi rest/stress imaging. A simultaneous ^{99m}Tc -Sestamibi/ ^{123}I -BMIPP protocol has many advantages: First, iodinated fatty acid analogs such as ^{123}I -BMIPP (^{123}I - β -methyl iodophenyl pentadecanoic acid) make possible the assessment of its metabolic state.^{1–5} Images of ^{123}I -BMIPP at rest provide an “ischemic memory,” which delineates segments of myocardium that have been starved of adequate blood supply (ischemic muscle) at significant time intervals after the event and which correlates with abnormal blood flow patterns typically observed by perfusion tracers during stress testing. Although ^{99m}Tc labeled perfusion agents are very sensitive for the detection of acute cardiac ischemia when injected during active chest pain, their sensitivity is significantly reduced when injected after the chest pain is resolved. In this context, metabolic tracers

such as ^{123}I -BMIPP (Refs. 2–4) appear very attractive because of their ability to delineate persistent posts ischemic changes in myocardial metabolism (ischemic memory). Second, the simultaneous protocol would yield “stress” and rest studies under identical conditions of patient motion, positioning, and attenuation paths. Eliminating the need for stress testing could also improve the sensitivity of identifying coronary artery disease, which is low in patients who are unable to achieve maximum predicted heart rate. The spatial registration of the reconstructed rest and stress images would be perfect, facilitating image interpretation. Third, the simultaneous protocol would obviate the need for patient exercise, a potentially harmful activity in those whose cardiac function is compromised, making it an ideal protocol for the emergency department setting. Fourth, a single acquisition would obviate the need for separate rest/stress protocols, improving the efficiency of nuclear cardiology laboratories.

Separation of ^{99m}Tc and ^{123}I images is difficult because

TABLE I. Data sets acquired. Multiple acquisitions were acquired for each data set. Each acquisition consisted of 32 rotation steps, and data were collected for 35 s at each angle. The total counts for each data set given in the table are the summed counts from all the acquisitions for the data set.

Data set	Total counts ($\times 10^6$)
^{99m}Tc myocardium–empty-phantom	35.0
^{99m}Tc myocardium	35.8
^{99m}Tc liver	55.5
^{99m}Tc background	273.4
^{123}I myocardium–empty-phantom	13.1
^{123}I myocardium	58.0
^{123}I liver	42.5
^{123}I background	114.6

their emission energies are close. Not only are downscattered ^{123}I photons detected in the ^{99m}Tc window but, equally important, primary photons of each radionuclide are detected in the wrong window (cross talk), making the discrimination between them on the basis of energy challenging. Constrained spectral factor analysis and artificial neural network are two promising approaches to compensate for scatter, cross talk, and high-energy septal penetration in simultaneous $^{99m}\text{Tc}/^{123}\text{I}$ imaging and have been recently tested successfully in clinical brain studies.^{6–9} The relative bias of activity estimation in brain structures is generally less than 10%. However, these methods generally require many energy windows.

A group at the Utrecht University Medical Center recently developed promising acceleration techniques based on the use of “scatter maps” and convolution forced detection.^{10–12} We have previously extended their research and developed a fast Monte Carlo (MC) simulation method to accurately model all physical factors involved in image formation while also incorporating patient-specific activity distributions. This algorithm was incorporated into a joint ordered-subset expectation maximization (JOSEM) approach, denoted MC-JOSEM,^{13,14} in order to compensate simultaneously for scatter and cross talk, as well as for collimator penetration and collimator and detector scatters. In the past, we have applied MC-JOSEM to Monte Carlo simulated dual-radionuclide $^{99m}\text{Tc}/^{123}\text{I}$ brain data¹⁴ and simulated and experimental ^{111}In data^{13,15} and have found that MC-JOSEM is superior to OSEM with energy window-based scatter correction. In this work, we evaluated the performance of our MC-JOSEM approach in $^{99m}\text{Tc}/^{123}\text{I}$ studies acquired using a cardiac torso phantom, a Siemens e.cam SPECT system, and a

GE PET/CT system (only CT used) and compared its performance with two conventional approaches: (1) standard OSEM using photopeak energy windows without scatter correction (NSC-OSEM) and (2) standard OSEM using an optimized Compton-scatter energy window for scatter correction (SC-OSEM).

II. METHODS

II.A. Data acquisitions

We used a dual-head Siemens e.cam system equipped with low-energy high-resolution (LEHR) collimators for data acquisitions. The standard clinical cardiac protocol with a 90° detector configuration was used. The camera was operated in a “step and shoot” mode, with both detectors rotated 90° with 32 steps and data acquired for 35 s at each angle in each acquisition. There were a total of 64 views covering a 180° angular range in each acquisition, and each projection was a 64×64 matrix with a pixel size of $6.6 \times 6.6 \text{ mm}^2$ (zoom factor: 1.455). In the protocol, both the horizontal gantry position and the vertical patient bed position were adjusted according to the phantom contour so that the detectors were positioned as close to the heart as possible. Therefore, the distances from the center of the imaging volume to the detectors were changing at each view. We acquired data in frame mode for four energy windows: 90–120 keV (the scatter window used for SC-OSEM only), 129–148 keV (the ^{99m}Tc photopeak window), 148–175 keV (the ^{123}I photopeak window), and 189–199 keV (the ^{123}I high-energy-photon calibration window).

A Data Spectrum anthropomorphic torso phantom with cardiac insert was used for all the acquisitions. This phantom includes heart (myocardium wall and myocardium cavity), left and right lungs, liver, spine, and a soft tissue compartment. For all the acquisitions, there was no radioactivity in the lungs (filled with Styrofoam beads), the spine, and the cavity of the heart (always filled with water). The phantom was always placed at the same position on the bed. By placing several marks on the phantom and on the bed, we achieved a repositioning accuracy of $\pm 1 \text{ mm}$. The trajectory of the two detectors was the same for all acquisitions. The distance from the center of rotation to either detector ranged from 17.8 to 25.8 cm. Virtually noise-free data were acquired for ^{99m}Tc and ^{123}I separately. For each radionuclide, we acquired the following four data sets (summarized in Table I).

(1) Myocardium–empty-phantom: The myocardium wall

TABLE II. Activity concentration ratios for different activity combinations.

Combination	^{99m}Tc :myocardium/ background	^{99m}Tc :liver/ background	^{123}I :myocardium/ background	^{123}I :liver/ background	^{99m}Tc :background/ ^{123}I : background
C1	6	3	6	3	1
C2	3	3	6	3	1
C3	6	3	3	3	1
C4	3	3	3	3	1

was filled with radioactive water. Both the liver and the soft tissue background compartments were empty (air).

- (2) Myocardium: The myocardium wall was filled with radioactive water. The liver and the soft tissue background compartments were filled with “cold” water. The *myocardium-empty-phantom* and *myocardium* data sets were acquired sequentially using the same radioactive water.
- (3) Liver: The liver compartment was filled with radioactive water. The myocardium wall and soft tissue background compartments were filled with cold water.
- (4) Background: The soft tissue background compartment was filled with radioactive water. The liver and the myocardium wall compartments were filled with cold water.

From myocardium, liver, and background data sets, we generated four different activity combinations as shown in Table II using different ^{99m}Tc myocardium wall/background and ^{123}I myocardium wall/background concentration ratios. For each activity combination, we created two virtually “noise-free” projection sets: one was a mix of liver and background data sets (liver+background) and the other was a mix of myocardium, liver, and background data sets (myocardium+liver+background). Each original data set was scaled before mixing to account for radioactive decay, scan time, and injected activity (measured by a dose calibrator). The synthesized projection data sets were then scaled again to yield a clinically realistic number of counts, i.e., 12×10^6 total counts in the 129–148 keV window from ^{99m}Tc -only data for the myocardium+liver+background combinations. We then generated 16 noise realizations from each noise-free myocardium+liver+background and liver+background combinations of projection data.

Two CT acquisitions of the phantom with the water-filled heart installed (one with water in liver and background and the other with empty liver and background compartments) were also acquired on a GE PET/CT scanner. They were later registered to the SPECT image reconstructed from noise-free myocardium+liver+background using mutual information. Because the phantom was always placed at the same position on the e.cam bed, the registered CT images are therefore registered to all the SPECT images. The CT bed in the CT images was digitally replaced with the e.cam bed. The CT images were used for accurate modeling of attenuation and scatter media during the fast MC simulation and image reconstruction.

II.B. Reconstructions

We first used ^{99m}Tc -only and ^{123}I -only myocardium-empty-phantom data sets to reconstruct the “true” ^{99m}Tc and ^{123}I images. Photopeak projection data were first used to reconstruct images using OSEM. The reconstructed images were then used by the fast MC as the starting images to obtain scatter estimates. Finally, the OSEM reconstruction was continued but now using the scatter and cross-talk estimates obtained from the fast MC during each forward-

projection process. The images after 100 iterations were used as the “truth” images. The above procedures were performed separately for ^{99m}Tc and ^{123}I data.

For each of the 16 noise realizations and for the noise-free projection data for each activity combination (both liver+background and myocardium+liver+background), we used the following reconstruction schemes.

- (1) The photopeak-energy-window projections (129–148 keV for ^{99m}Tc and 148–175 keV for ^{123}I) were reconstructed independently using standard OSEM while modeling the attenuation map and the collimator-detector PSF but without scatter correction. This method is illustrated in Fig. 1 and denoted NSC-OSEM (for “no scatter correction” OSEM).
- (2) The photopeak and scatter images were reconstructed separately in the ^{99m}Tc photopeak window and scatter window (90–120 keV) using the standard OSEM. The scatter images were then scaled by a factor of $k=0.6$ and subtracted from the photopeak images to obtain the final ^{99m}Tc images. The scaling factor was chosen so that the activity in a selected region in the lungs was minimized as no activity existed in the lungs. This method is denoted SC-OSEM.
- (3) The ^{99m}Tc and ^{123}I images after five iterations of NSC-OSEM were used as starting images for the fast MC algorithm to estimate scatter and cross-talk contributions to both photopeak energy windows. Fifty million photon histories were generated based on these two starting images to estimate scatter contributions for each of the 64 projection angles. We simulated scatter maps at each projection angle for many energy windows, denoted as object energy windows (OEWs), throughout the entire energy spectrum for all the primary and scattered photons that have non-negligible probability of being detected in the two detected energy windows (DEWs) used by the scanner. These scatter maps were then blurred by the PSFs to form the projection for each DEW to obtain

FIG. 1. Flow chart of NS-OSEM, MC-JOSEM (1), and MC-JOSEM (2).

the scatter and cross-talk estimates. Then, a joint OSEM incorporating two radionuclides and two DEWs was performed with 100 additional iterations for noise-free projection and 30 iterations for each noise realization. The simulated PSFs and attenuation corrections were included in both the forward projection and backprojection. The fast MC-estimated scatter contributions, which were calculated only once, were added to the estimates of primary photon projections during the forward-projection step of each iteration. For the joint OSEM, each forward projection has contributions from both isotopes, in which each backprojection has contribution from both DEWs. This is different from the standard OSEM procedure, in which only one radionuclide and one DEW are involved in the reconstruction process. This algorithm is illustrated in Fig. 1 and denoted as MC-JOSEM (1).

- (4) The same procedures as in scheme (3) except the reconstructed ^{99m}Tc and ^{123}I images from the 100th iteration of MC-JOSEM (1) were used as the starting images by the fast MC algorithm. This algorithm is illustrated in Fig. 1 and denoted MC-JOSEM (2). This was only performed for the noise-free projection data.

The detector point spread functions (PSFs) were simulated separately for a sphere source in air. All the physical processes in the detector materials, including penetration and scatter in the collimator, the NaI(Tl) crystal, and the materials behind the crystal, were modeled. A single-layer “effective” backscatter compartment, which has a thickness of 6.6 cm and a density of 66% of that of Pyrex, was used to model all the materials behind the crystal.¹⁶ The sphere source has the same volume as a voxel (287.5 mm³). The PSFs were represented by a five-dimensional array indexed by OE, DEW, source to collimator distance (32 bins from 0.4 to 63.6 cm), and a two-dimensional detector “kernel” (6.6 × 6.6 mm² sampling). Each kernel was represented by a 31 × 31 pixel array; however, only one 16 × 16 quadrant needed to be stored owing to symmetry.

For all reconstructions in this study, eight subsets were used with eight projections per subset. In both the projector and backprojector, the attenuation map and the detector PSF were modeled. The reconstructed image volume consisted of 64 × 64 × 64, 6.6 mm cubic voxels.

As described in Ref. 14, we defined 13 OEWs each 4.25 keV wide and 2 OEWs each 2 keV wide (these two 2 keV bins were used for ^{99m}Tc and ^{123}I photopeaks): 100.75–105.00, 105.00–109.25, 109.25–113.50, 113.50–117.75, 117.75–122.00, 122.00–126.25, 126.25–130.50, 130.50–134.75, 134.75–139.00, 139.00–141.00, 141.00–145.25, 145.25–149.50, 149.50–153.75, 153.75–158.00, and 158.00–160.00 keV. Either a primary (excluding ^{123}I photons with energies higher than 159 keV) or a scattered photon with energy within the range covered by these energy windows will have negligible chance to be detected. We defined two DEWs: 129–148 and 148–175 keV.

Low-abundance photons emitted by ^{123}I with energies higher than 159 keV contribute a broad, slowly varying

background to projection images. The projection profile from these high-energy ^{123}I photons is, to a good approximation, independent of detected energy window (for energies less than 200 keV).⁷ In Ref. 7, the projection profile from these high-energy ^{123}I photons was also found to be independent of projection angles because a brain phantom was used and the radius of the detector orbit remained constant for each view. We have found that this is not the case for this study and the projection profile at different projection angles is very different. In order to understand how the intensity is related to energy and projection angle, we performed a full simulation of the phantom while generating only ^{123}I photons with energies higher than 160 keV. We found that the intensity is energy dependent and could be modeled using this ^{123}I high-energy-photon-only simulation. Based on these results, we used the projection acquired with energy window of 189–199 keV to obtain a smooth projection distribution of ^{123}I high-energy-photon background per keV, Y , for each data set. For each energy window used in the image reconstruction, the contribution from ^{123}I high-energy photons is $\Delta E^l \beta^l Y$, where ΔE^l is the energy window size in keV for energy window indexed by l and β^l is a scaling factor which accounts for the energy dependence of intensity. From the simulation of ^{123}I high-energy photons alone, we calculated the following values for β^l : 1.08 and 1.16 for energy windows 129–148 and 148–175 keV, respectively. Because we do not expect β^l to change much for different patients, it is not necessary to simulate ^{123}I high-energy photons and obtain a separate β^l for each patient study. In MC-JOSEM, ^{123}I high-energy photons were not generated in the fast MC simulation; instead, the estimates were added separately during forward projecting.

II.C. Evaluation

For each method, a “difference image” was obtained by subtracting the liver+background image from the myocardium+liver+background image at each iteration. This difference image was compared with the truth image in the myocardium wall. We calculated relative bias (RB) and relative standard deviation (RSD) as

$$\text{RB} = \frac{w^{\text{nf}} - t}{t}, \quad \text{RSD} = \frac{\sqrt{\text{Var}}}{t}, \quad (1)$$

where w^{nf} is the total counts for myocardium wall in the difference image obtained from noise-free projection data, t is the true counts from the reconstructed image of the empty phantom data, and Var is the variance calculated from 16 difference images, reconstructed from the 16 noise realizations. For both the reconstructed ^{99m}Tc and ^{123}I images, we also calculated the myocardium wall to cavity contrast, which is defined as

$$C = (m_{\text{myocardium}} - m_{\text{cavity}})/m_{\text{myocardium}}. \quad (2)$$

Objective task-based assessment of the performance of MC-JOSEM was achieved by comparing the activity concentration estimation precision for both radionuclides with ideal performance, representing the best theoretical performance

FIG. 2. Comparison of reconstructed images after 40 iterations. The images in the top and bottom rows are for ^{99m}Tc and ^{123}I , respectively. The images from the first column were reconstructed from myocardium-empty-phantom projection data, which were properly scaled to activity combination C1 by MC-JOSEM. The images in the second, third, fourth, and fifth columns were reconstructed from noise-free projection data from C1 by NSC-OSEM, SC-OSEM (^{99m}Tc only), MC-JOSEM (1), and MC-JOSEM (2), respectively.

for the system. We first evaluated the precision expected by an unbiased and efficient estimator¹⁷ by calculating the Cramer–Rao lower bound (CRB) on ^{99m}Tc and ^{123}I activities in the myocardium wall using the same noise-free acquisitions, energy windows, and target to background activity ratios as were used in the MC-JOSEM reconstruction. To calculate the CRB on myocardium wall activity, we first generated 11 PSFs by simulating projections of 11 point sources distributed across the myocardial wall in the water-filled phantom to account for spatial variation of the PSF. We then modeled analytic myocardial projections convolved with these Monte Carlo simulated point spread functions and added these to the liver+background acquisitions. A distance-weighted convolution was then performed at each point of the myocardium projection (PSFs generated spatially near to the point were more favorably weighted). Then, we evaluated an approximation of the biased CRB by taking the bias into account.¹⁸ The biased bound is specific to the

estimator used and represents the best performance (minimum mean square error) for that estimator. It is calculated by computing the derivative of the bias with respect to the parameter of interest (activity concentration in this case). We calculated the bias for two values of activity concentration that were close in value and used a simple linear fit to compute the approximate bias derivative. Both the unbiased and biased CRBs were compared with the relative standard deviation to mean (RSDM) obtained using the 16 noise realizations for each activity combination. We calculated RSDM as

$$\text{RSDM} = \frac{\sqrt{\text{Var}}}{m}, \quad (3)$$

where m is the mean count for myocardium for the 16 noise realizations.

FIG. 3. Comparison of reconstructed short-axis slices after 40 iterations. These slices are from the same image volumes described in Fig. 2.

FIG. 4. Relative bias of activity estimates for C1–C4.

III. RESULTS AND DISCUSSION

Figure 2 shows a transverse midmyocardium slice through the phantom from an image volume reconstructed from noise-free projections of activity combination C1 by NSC-OSEM, SC-OSEM (for ^{99m}Tc only), and MC-JOSEM algorithms after 40 iterations. It also shows the truth images, which were reconstructed separately for ^{99m}Tc and ^{123}I from

properly scaled myocardium–empty-phantom projection data by MC-JOSEM after 40 iterations. Figure 3 shows one short-axis slice from the same image volume. Because NSC-OSEM does not include scatter and cross-talk corrections, the cold regions including the myocardium cavity, the spine, and the lungs still have significant number of voxels that have nonzero values. For the same reason, myocardium wall

TABLE III. Relative bias of ^{99m}Tc activity estimates in the myocardium wall for different combinations after 100 iterations.

Combination	NSC-OSEM (%)	SC-OSEM (%)	MC-JOSEM (1) (%)	MC-JOSEM (2) (%)
C1	37.0	19.3	12.1	7.5
C2	55.8	31.5	19.1	13.5
C3	27.6	13.2	7.9	4.0
C4	37.1	19.4	10.3	7.2

TABLE IV. Relative bias of ^{123}I activity estimates in the myocardium wall for different combinations after 100 iterations.

Combination	NSC-OSEM (%)	MC-JOSEM (1) (%)	MC-JOSEM (2) (%)
C1	22.9	−2.4	−3.6
C2	19.3	0.8	−1.2
C3	29.8	−8.7	−7.1
C4	22.6	−2.6	−3.0

FIG. 5. Relative standard deviation of activity estimates for combinations C1–C4.

in the images reconstructed by NSC-OSEM shows much higher activity than the true value. The images reconstructed by SC-OSEM become more accurate but slightly noisier. By modeling scatters inside the phantom and incorporating accurate detector PSFs, MC-JOSEM produced more accurate

and precise images than those reconstructed by both NSC-OSEM and SC-OSEM. This is confirmed by the quantitative results described below.

Using the myocardium–empty-phantom data as reference, Fig. 4 shows the relative bias of the reconstructed ^{99m}Tc and ^{123}I activities in the myocardium versus the iteration number,

TABLE V. Relative standard deviation of ^{99m}Tc activity estimates in the myocardium wall for different combinations after 30 iterations.

Combination	NSC-OSEM (%)	SC-OSEM (%)	MC-JOSEM (1) (%)
C1	1.1	1.3	0.8
C2	1.3	1.5	0.8
C3	0.8	0.8	0.5
C4	1.1	1.5	0.8

TABLE VI. Relative standard deviation of ^{123}I activity estimates in the myocardium wall for different combinations after 30 iterations.

Combination	NSC-OSEM (%)	MC-JOSEM (1) (%)
C1	1.1	0.8
C2	0.8	0.7
C3	1.6	1.3
C4	1.3	1.1

FIG. 6. Myocardium wall to cavity contrast for combinations C1–C4.

respectively. For ^{99m}Tc activity estimate, the NSC-OSEM yielded the largest relative bias because the ^{99m}Tc photopeak energy window contains contamination from both ^{123}I down-scatter and ^{99m}Tc scatter. The relative bias was less with SC-OSEM because an estimate of the scatter contamination was used. Using the reconstructed images from NSC-OSEM as the starting images for the fast MC, MC-JOSEM (1)

yielded less bias than both NSC-OSEM and SC-OSEM. The relative bias was further reduced with MC-JOSEM (2) using the reconstructed images from MC-JOSEM (1) as starting images for the fast MC. For ^{123}I activity estimate, there was no notable improvement from MC-JOSEM (1) to MC-JOSEM (2). However, they both yielded lower relative bias than NSC-OSEM. Given the fact that the improvement of

TABLE VII. Myocardium wall to cavity ^{99m}Tc contrast for different combinations after 100 iterations.

Combination	NSC-OSEM	SC-OSEM	MC-JOSEM (1)	MC-JOSEM (2)
C1	0.88	0.97	0.99	0.98
C2	0.84	0.94	0.98	0.98
C3	0.90	0.98	0.99	0.99
C4	0.88	0.97	0.98	0.98

TABLE VIII. Myocardium wall to cavity ^{123}I contrast for different combinations after 100 iterations.

Combination	NSC-OSEM	MC-JOSEM (1)	MC-JOSEM (2)
C1	0.92	0.99	0.99
C2	0.91	0.99	0.99
C3	0.92	0.99	0.98
C4	0.92	0.99	1.00

TABLE IX. Relative standard deviation to mean (RSDM) of ^{99m}Tc activity estimates after 30 iterations versus both nonbiased and biased CRBs from MC-JOSEM (1). The relative bias at the same iteration was used to calculate the biased CRB.

Combination	Unbiased CRB (%)	Biased CRB (%)	RB (%)	RSDM (%)
C1	0.26	0.19	7.5	0.8
C2	0.48	0.34	11.9	0.7
C3	0.26	0.20	3.3	0.5
C4	0.47	0.39	3.1	0.8

MC-JOSEM (2) over MC-JOSEM (1) is minor based on our phantom studies and MC-JOSEM (2) requires significant extra computing time, it seems that MC-JOSEM (2) is not needed. However, we believe that the performance of MC-JOSEM (2) should be further evaluated using patient data.

The values of relative bias of the ^{99m}Tc and ^{123}I activity estimates in the myocardium wall after 100 iterations are shown in Tables III and IV, respectively. On average, the relative biases were 8.1% for ^{99m}Tc (ranged from 7.2% to 13.5%) and 3.7% for ^{123}I (ranged from -7.1% to -1.2%) with MC-JOSEM, 20.9% for ^{99m}Tc (ranged from 13.2% to 31.5%) with SC-OSEM, and 39.4% for ^{99m}Tc (ranged from 27.6% to 55.8%) and 23.7% for ^{123}I (ranged from 19.3% to 29.8%) with NSC-OSEM. Because the cross talk between the two radionuclides was not perfectly modeled (for example, the errors introduced by inaccurate starting images used by the fast MC and approximation made on collimator penetration from high-energy ^{123}I photons), notable bias still exists. Whenever one radionuclide had a higher concentration in the myocardium wall relative to the other radionuclide, the bias for the other radionuclide was higher. For example, C2 (C3) had the lowest (highest) concentration ratio between ^{99m}Tc and ^{123}I in the myocardium wall (see Table II), and the relative bias for ^{99m}Tc was the highest (lowest) for every method. This was also true for ^{123}I .

Figure 5 shows the relative standard deviation of the ^{99m}Tc and ^{123}I activity estimates in the myocardium, respectively, versus the iteration number. SC-OSEM yielded higher relative standard deviation than NSC-OSEM since the counts in the scatter energy window were subtracted from the photopeak window. On the other hand, MC-JOSEM consistently yielded the lowest relative standard deviation values at all iteration numbers for both ^{99m}Tc and ^{123}I activity estimates. The statistical variance introduced by fast MC is negligible because a large number of photon histories were simulated and all the interaction points in each photon history were used to populate projections. Therefore, RSDM for both NSC-OSEM and MC-JOSEM should be close. Given the higher positive bias from NSC-OSEM as compared with MC-JOSEM, MC-JOSEM therefore produced lower RSD. We did not calculate the standard deviation from MC-JOSEM (2) because it required significant computing time and it is not expected to improve precision as compared with MC-JOSEM (1).

The values of relative standard deviation of the ^{99m}Tc and

TABLE X. Relative standard deviation to mean (RSDM) of ^{123}I activity estimates after 30 iterations versus both nonbiased and biased CRBs from MC-JOSEM (1). The relative bias at the same iteration was used to calculate the biased CRB.

Combination	Unbiased CRB (%)	Biased CRB (%)	RB (%)	RSDM (%)
C1	0.19	0.19	-6.6	0.9
C2	0.19	0.20	-3.6	0.7
C3	0.31	0.37	-13.9	1.5
C4	0.31	0.37	-8.4	1.2

^{123}I activity estimates in the myocardium wall after 30 iterations are shown in Tables V and VI, respectively. By averaging the results reported in the tables over all activity combinations, we have achieved relative standard deviations of 0.7% (ranged from 0.5% to 0.8%) for ^{99m}Tc and 1.0% (ranged from 0.7% to 1.3%) for ^{123}I with MC-JOSEM (1) as compared to 1.1% (ranged from 0.8% to 1.3%) for ^{99m}Tc and 1.2% (ranged from 0.8% to 1.6%) for ^{123}I with NSC-OSEM and 1.3% (ranged from 0.8% to 1.5%) for ^{99m}Tc with SC-OSEM.

Figure 6 shows the myocardium wall to cavity contrast for both ^{99m}Tc and ^{123}I . As expected, MC-JOSEM yielded better contrast than NSC-OSEM and SC-OSEM after enough number of iterations. After 100 iterations, the contrast from either MC-JOSEM (1) or MC-JOSEM (2) is very close to the theoretical limit. The values of myocardium wall to cavity ^{99m}Tc and ^{123}I contrast after 100 iterations are shown in Tables VII and VIII, respectively. After converging, the myocardium wall to cavity contrast with MC-JOSEM was close to 1.

Table IX (Table X) shows the unbiased and biased CRBs together with the relative standard deviation to mean [same as RSD defined in Eq. (1) except mean was used in the denominator to include the effects of bias] of ^{99m}Tc (^{123}I) activity estimates in the myocardium wall after 30 iterations. The relative bias after 30 iterations, which are shown in the tables, was used to calculate the biased CRB. The measured precision, which was much less than the measured bias, was slightly above the biased CRB. The biased bound is directly comparable to the measured precision because it takes into account the bias in the method. The unbiased CRB is shown to exemplify the effect of bias on theoretical precision. For this estimator, the bias decreased the theoretical precision values for the ^{99m}Tc activity estimates but slightly increased them for the ^{123}I estimates. For both radionuclides, the biased bound was two to four times lower than the measured precision, suggesting that the method could be further improved. It should be noted, however, that the biased bounds were computed by taking a finite difference at two closely valued activity concentrations, and therefore are only approximations.

We have studied the performance for NSC-OSEM, SC-OSEM, and MC-JOSEM on an AMD 2.4 GHz Opteron processor. For both NSC-OSEM and SC-OSEM, which use single isotope and single energy window reconstruction, it

takes about 2 min for each iteration for each radionuclide. For MC-JOSEM, which relies on start images from NSC-OSEM, it takes an extra 60 min for the fast MC simulation (using 50×10^7 photon histories), 5 min for convolution, and 5 min per iteration for JOSEM. In the future, we expect to make further improvement on the performance of MC-JOSEM. In the current implementation of MC-JOSEM, projection and backprojection are performed at each projection angle while the image volume is fixed in space. We believe that we can save significant computing time by rotating the image volume so that pixels in the detector plane are aligned with voxels in the imaging volume while keeping the detector plane fixed in space. The computing time for image rotation can be significantly reduced by precalculating and storing the rotation matrix, which is uniform along the axial direction. The stored rotation matrix data will be loaded before MC-JOSEM is launched and can make rotation much faster to calculate. Additionally, when we have alignment between pixels and voxels, calculations of projection and backprojection are much faster. We can also use a computer cluster to reduce the computing time significantly by parallelizing both the fast MC simulation and iterative reconstruction.

IV. CONCLUSIONS

We have applied MC-JOSEM to $^{99m}\text{Tc}/^{123}\text{I}$ cardiac experimental data and compared its performance with that of two conventional methods: NSC-OSEM and SC-OSEM. We have achieved improved performance with MC-JOSEM on relative bias, relative standard deviation, and myocardium wall to cavity contrast for both radionuclides compared these other techniques. We then compared the results of our method with the unbiased and biased Cramer–Rao lower bounds, representing the theoretical minimum variance on activity estimation, and demonstrated that the method could be further improved to attain the biased bound on estimation. Future studies include the assessment of myocardial defect detectability, heart motion correction, and impact of patient size.

ACKNOWLEDGMENTS

This work was supported by NIH Grant Nos. RO1-EB005876 and RO1-EB001989. Part of the image reconstructions for this paper was performed on a cluster supported by a Society of Nuclear Medicine Pilot Research Grant.

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