Phantom and clinical evaluation of bone SPECT/CT image reconstruction using novel conjugate gradient method

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Noriaki Miyaji
Department of Nuclear Medicine, Cancer Institute Hospital of Japanese Foundation for Cancer Research

Kenta Miwa
Department of Radiological Sciences, School of Health Science, International University of Health and Welfare

Ayaka Tokiwa
Department of Radiological Sciences, School of Health Science, International University of Health and Welfare

Hajime Ichikawa
Department of Radiology, Toyohashi Municipal Hospital

Takashi Terauchi
Department of Nuclear Medicine, Cancer Institute Hospital of Japanese Foundation for Cancer Research

Misturu Koizumi
Department of Nuclear Medicine, Cancer Institute Hospital of Japanese Foundation for Cancer Research

Masahisa Onoguchi
Department of Quantum Medical Technology, Graduate school of Medical Sciences, Kanazawa University

onoguchi@staff.kanazawa-u.ac.jp

Corresponding Author

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Abstract

Background

Two novel methods of image reconstruction, xSPECT Quant (xQ) and xSPECT Bone (xB) that use an ordered subset conjugate gradient minimizer (OSCGM) for bone SPECT/CT have been proposed. The present study compares the performance characteristics of xQ, xB and conventional Flash3D (F3D) reconstruction using images derived from phantoms and patients.

Methods

A custom-designed body phantom for bone SPECT was scanned using a Symbia Intevo (Siemens Healthineers) and reconstructed xSPECT images were evaluated. A phantom with 28-mm spheres containing a 99m Tc background, and having tumor-to-bone ratios (TBR) of 1, 2, 4 and 10, was evaluated as the convergence of 1 - 96 iterations. The full width at half maximum (FWHM) of a simulated spinous process (10 mm), coefficients of variance (CV) and recovery coefficients (RC) of a simulated spine on SPECT images determined using F3D, xQ, xB were compared in a phantom containing four spheres with diameters of 13, 17, 22, 28 mm at TBR4 containing a 99m Tc-background. Images from 20 patients with suspected bone metastases (male, n = 13) were acquired using 99m Tc-(H)MDP SPECT/CT, then the CV and standardized uptake value (SUV) at the 4 th vertebral body (L4) were compared with xQ and xB in a clinical setup.

Results

Mean radioactive concentrations with various TBR converged in accordance with increasing numbers of iterations. Spatial resolution was improved in the order of xB, xQ and F3D regardless of the number of iterations during reconstruction. The CV and RC were better for xQ and xB than F3D. The RC significantly differed between xQ and xB at lower numbers of iterations, whereas those of xQ and xB became almost saturated at higher iteration numbers. The CV and SUV for clinical patients did not significantly differ between xQ and xB.

Conclusions

The reconstructed xQ and xB images were better than those conventionally reconstructed using F3D. Bone SPECT xB imaging offered essentially unchanged spatial resolution even when the numbers of
iterations did not converge. The xB further enhanced SPECT image quality using CT data. Our findings provide important evidence for understanding the performance characteristics of the novel xQ and xBalgorithms.

**Background**

Traditional bone scans (BS) using $^{99m}$Tc-labeled phosphate compounds are widely applied as diagnostic tools for detecting osseous metastases and staging malignant disease [1–3]. Hybrid imaging using single photon emission computed tomography/computed tomography (SPECT/CT) for BS, can enhance image quality due to attenuation correction (AC) and scatter correction (SC) and tracer uptake is precisely localized. Römer et al. showed that 92% of indeterminate lesions could be correctly classified by SPECT/CT with a pronounced benefit for bone lesions [4]. Utsunomiya et al. also reported significantly improved diagnostic confidence for fused SPECT/CT image datasets compared with side-by-side views of images from both modalities [5]. Hybrid SPECT/CT imaging has overcome the problem of BS, which has high sensitivity but low specificity, and thus improves the accuracy of diagnosing bone lesions [6, 7].

Recent advances in SPECT technology have included not only hardware but also software, including image reconstruction. Absolute quantitation of $^{99m}$Tc bone SPECT/CT has become important as a diagnostic tool and as a means of monitoring treatment effects [8, 9]. Previous phantom and clinical studies have found that the quantitative accuracy of SPECT imaging using $^{99m}$Tc is within $±10\%$ [10, 11]. A multicenter study of four SPECT-CT systems has achieved quantitative error within 10%, using 3D iterative reconstruction with attenuation, scatter correction and resolution recovery [12]. Although further study and technological advancements are needed before quantitative bone SPECT imaging could become a feasible tool for clinical applications, the need and importance of developing novel SPECT imaging techniques associated with absolute SPECT quantitation have been discussed [13–15]. Improved spatial resolution of SPECT images helps quantitative improvement as well as the detection and precise localization of small lesions [16]. However, the spatial resolution of SPECT images remains limited. Tsui et al. suggested that multimodal image reconstruction would remarkably improve SPECT image quality [17]. Kuwert et al. also focused on quantitation and the above
reconstruction technique as a methodological advance to further improve the value of bone SPECT/CT imaging [13]. The impact of SPECT imaging caused by this reconstruction should be verified, but SPECT imaging using novel reconstruction methodology should be more quantifiable and have excellent diagnostic confidence.

Siemens® has introduced a technology called “xSPECT”, which includes a novel iterative image reconstruction algorithm (ordered subset conjugate gradient minimizer; OSCGM) based on the conventional ordered subset expectation maximization (OSEM; Flash 3D; F3D) to improve multimodal alignment in image space, and thus enhance image quality. Onoguchi et al. have described the differences between OSEM and OSCGM algorithms in detail [18]. Briefly, the xSPECT technology applies the Mighell merit function to suppress noise caused by the fast convergence of OSCGM reconstruction. This method of quantitative reconstruction is called “xSPECT Quant” (xQ). Siemens® also concurrently released bone-specific software with xSPECT features called “xSPECT Bone (xB)” [19], in which higher-resolution CT data have been added to enhance reconstructed images at tissue boundaries. Therefore, xB produces images of tracer distribution with far better quality than F3D [20]. Some clinical reports have described that xB images for bone SPECT are more precise in terms of localization and offer better diagnostic confidence in staging malignant disease [21–23].

The fundamental theory of xSPECT is that the use of image space minimizes interpolation errors of information obtained from anatomical modalities, and reconstructed images have high spatial recognition due to denser spatial sampling. However, developers found that an unexpected behavior of xSPECT could arise with different reconstruction parameters [24]. Although quantitative and physical indexes such as recovery coefficients (RC), standardized uptake values (SUV) and noise characteristics depend on the method of SPECT image reconstruction and the reconstruction parameters, the impact of qualitative and quantitative xSPECT imaging has not been clarified. The present study aimed to determine the performance characteristics of the novel xSPECT algorithm. To our knowledge, this is the first attempt to clarify functional differences between xQ and xB using phantoms and a clinical approach.

Methods
Data acquisition and reconstruction
All imaging data were acquired using a Symbia Intevo16 hybrid SPECT/CT system (Siemens Healthineers, Erlangen, Germany) comprising an integrated dual-head SPECT camera with a 16-slice helical CT scanner. We acquired SPECT images under the following parameters: ±7.5% energy window at 140 keV with a lower scatter window of 15%, ⅜” crystal thickness, low-energy high-resolution collimator, 256 × 256 matrix with a 2.4-mm pixels and a total of 120 projections of 15 s/view over 360° in non-circular orbit continuous acquisition mode. Immediately following the SPECT acquisition, CT images were acquired at 130 KV and 70 ref mA using adaptive dose modulation (CARE Dose 4D; Siemens Healthineers) with a 512 × 512 matrix, pitch 1.5, 0.8-s rotation and 2 × 1.5-mm collimation. The CT data were reconstructed at a slice thickness of 3.0 mm using a B31s attenuation filter (Siemens Healthineers).

We reconstructed SPECT images using the algorithms F3D, xQ and xB and a 6-mm 3D-Gaussian filter with various combinations of one fixed subset and 1–96 iterations. The F3D is equipped with OSEM and depth-dependent 3D-resolution recovery using the Gaussian point-spread functions, AC and SC. The xQ and xB are equipped with OSCGM and depth-dependent 3D resolution recovery using AC and SC. The xB algorithm divides CT pixels into six tissue classes with smooth boundaries based on CT values or “zones” of air and lung, adipose, soft tissue, soft bone, cortical bone, metal material, and updates.

Cross-calibration of SPECT imaging
Reconstructed SPECT counts derived from F3D and xSPECT were converted to radioactivity concentrations based on a cross-calibration factor (CCF; obtained from the relationship between the reconstructed counts and radioactivity concentrations) and system planar sensitivity, respectively, for quantitative comparisons.

In SPECT images using F3D, a circular ROI to measure SPECT count density (counts/mL) was placed at the center of the cylindrical phantom on the central slice and at ± 1 and ± 2 slices from the center. The calibration factor was automatically calculated using GI-BONE (Aze Ltd., Tokyo, Japan) software as the ratio of the actual radioactivity concentration (measured by the dose calibrator) in the phantom at
the time of scanning, to the measured SPECT counts density per scan duration [25]. The actual SUV was calculated as:

Reconstruction using xQ and xB was designed to estimate images in units of Bq/mL that are converted by system planar sensitivity during data processing [20]. We automatically converted quantitative SPECT/CT data using MI Applications VB10 (Siemens Healthineers). System planar sensitivity was measured a traceable $^{57}$Co point source (National Institute of Standards and Technology; NIST) to realize accurate and reproducible quantitation [10, 26, 27].

**Phantom Studies**

**Phantom design**

We custom-designed a physical three-dimensional phantom to determine the bone SPECT-specific distribution of radioactivity and the linear attenuation coefficient (Fig. 1). This phantom simulates SPECT images of bone metastasis with a realistic abdomen contour [28]. The phantom contains a $^{99m}$Tc solution to simulate soft tissue, and the vertebral body, spinous and transverse process, tumor region contained a bone-equivalent solution of $K_2HPO_4$ and $^{99m}$Tc [29]. The phantom allows the consideration of photon scatter and attenuation caused by bones. The phantom experiments proceeded twice as follows. A body phantom with four 28-mm diameter spheres was set at tumor-to-normal bone ratios (TBR) of 1, 2, 4 and 10 at a normal bone radioactivity level of 50 kBq/mL. This phantom contained 8 kBq/mL of a $^{99m}$Tc solution as the background radioactivity of soft tissue. Another phantom included spheres with diameters of 13, 17, 22, 28 mm, and radioactivity concentrations of simulated tumor, normal bone and soft tissue at 8, 50 and 200 kBq/mL, respectively, that is, TBR4.

**Data Analysis**

The SPECT acquisition data in the first experiment were reconstructed using subset 1 and 1–96 iterations. We examined the effects of the reconstruction algorithms on various TBR in the 28-mm sphere, then determined and applied the clinical reconstruction parameter in accordance with the result of this convergence characteristic. Phantom images containing different sizes of simulated tumors were continuously analyzed in terms of the spatial resolution of a 10-mm spinous process, the
coefﬁcient of variance (CV) of the vertebral body and recovery coeﬃcient (RC) as quantitative parameters. We drew proﬁle curves on the spinous process, measured the full width at half maximum (FWHM), and evaluated the CV at an 80% circular regions of interest (ROI80%) placed at the center of the vertebral body. The RC were placed at circular ROI with diameters of 13, 17, 22, 28 mm. The CV was calculated as SD/mean, where SD represents the standard deviation of the ROI in the radioactive section and mean represents the mean SPECT value (kBq/mL) in the ROI.

Clinical study
Imaging protocol
We analyzed data from 20 consecutive patients who had undergone bone SPECT/CT imaging for metastatic prostate or breast cancer (male, n = 13; female, n = 7; median age, 62 y; range, 40–83 y; average weight, 65.2 ± 13.4 kg; range, 51.8–78.6 kg). Bone SPECT/CT imaging proceeded from the abdomen to the pelvis ~2.5–4 h after delivering an intravenous injection of 1003.4 ± 102.8 MBq ⁹⁹mTc-methylene diphosphonate (⁹⁹mTc-MDP, FUJIFILM Toyama Chemical Co. Ltd., Tokyo, Japan) or hydroxymethylene diphosphonate (⁹⁹mTc-HMDP, Nihon Medi-Physics Co. Ltd., Tokyo, Japan). The average amount of injected ⁹⁹mTc was 15.9 ± 2.8 (range, 13.1–18.7) MBq/kg. The Ethics Committee at the Cancer Institute Hospital of JFCR approved this clinical study (Approval no. 2015 – 1151). The results of this retrospective study did not influence further therapeutic decision-making.

Data analysis
The noise characteristics and quantitative performance of the clinical SPECT image were analyzed at the level of the 4th vertebral body (L4) [30]. We placed a ROI80% on the center of the axial slice in the vertebral body section, and a ROI80% exactly on the corresponding vertebral body in the central slice by following the CT boundaries of the fused SPECT/CT images. We then determined the SUV$_{\text{max}}$, SUV$_{\text{mean}}$ and SUV$_{\text{peak}}$ for the ROI80%. All these data were analyzed using PETSTAT software (AdIn Research Inc., Tokyo, Japan).

Statistical analysis
All SUV and CV indices in the xQ and xB groups were compared using paired T-tests. Values with P < 0.05 were considered signiﬁcantly different. These data were statistically analyzed using SPSS Statistics (IBM, Armonk, NY, USA).
Results

Phantom studies

Convergence for various TBR

Figure 2 shows the SPECT data reconstructed using between 1 and 96 iterations. Regardless of the reconstruction model and iteration number, the maximum and mean radioactive concentrations were overestimated and underestimated when the TBR were respectively low and high. The mean radioactive concentration converged with increasing iterations regardless of the TBR. The mean radioactive concentrations of xQ and xB were essentially equivalent at > 24 iterations. The mean radioactive concentration was lower for F3D than xQ and XB.

Spatial resolution

Figure 3 shows the spatial resolution of the spinous process for various iterations. The FWHM with xQ and F3D improved considerably when the iteration number increased, but the spatial resolution with the xB algorithm was the best. The FWHM of the xQ and F3D reconstructions converged at about 15 and 20 mm, respectively. In contrast, the xB values remained similar to the actual size (10 mm) regardless of iterations. Figure 4 shows the results of the SPECT images with 48 iterations according to each reconstruction model. The reconstructed F3D and xQ bone SPECT images were visually indistinct, whereas the boundary between normal bone and the hot sphere was obvious in the reconstructed xB images. Both xB and F3D were visually clearer than xQ in terms of background noise.

Noise characteristics

Figure 5 shows the CV of the vertebral body according to the number of iterations. Although the CV increased in the order of xB, xQ and F3D as the number of iterations increased, the amount of noise was similar between xQ and xB. The CV of xQ and xB at > 24 iterations were both relatively stable at 0.2.

Recovery coefficient

Figure 6 shows the RC of vertebral body for 12 - 96 iterations. The RC in all algorithms improved with increasing sphere size. The RC was relative higher with the xB, than the other algorithms at 12 iterations, and differences in the RC between xQ and xB were essentially equivalent as a function of increasing numbers of iterations. The RC was lower for F3D than xQ and XB regardless of the
increasing number of iterations.

Clinical study
Figure 7 shows the typical $SUV_{\text{max}}$ and CV under clinical conditions. The $SUV_{\text{max}}$ was much higher for patient 15 and the CV was slightly higher for patients 14 and 16 than those of the others. The statistical findings showed that the noise characteristics and quantitative SPECT values between xQ and xB were similar, and that the $SUV_{\text{max}}$, $SUV_{\text{mean}}$, $SUV_{\text{peak}}$ and CV on SPECT images reconstructed using xQ and xB did not significantly differ.

Discussion
We validated novel xSPECT and conventional F3D reconstruction using experimental data derived from phantoms and clinical data derived from patients. The experimental findings indicated that the image quality and quantitative accuracy of xSPECT exceeded those of F3D. We also found that xB can maintain high spatial resolution even at various numbers of iterations. The clinical study did not identify any significant differences in the CV and the SUV between xQ and xB, but xB further enhanced bone SPECT images in terms of spatial resolution.

Regardless of the reconstruction models, the impact of statistical noise theoretically increased with lower counts. In fact, suppressing noise caused the maximum radioactivity concentration in the highest TBR to almost reach the actual radioactive concentration (Fig. 2). In contrast, the average activity concentration approached the true value at lower TBR. This can be explained by the lack of a partial volume effect because the radioactivity concentrations inside and outside the ROI were the same when TBR and BG were equal (TBR = 1). On the other hand, the radioactive concentration decreases as a result of spillage from within a hot sphere to the background, which raises the TBR [31]. Nevertheless, TBR 1 was slightly overestimated due to the radioactivity concentration being increased by statistical noise. The quantitative differences between F3D and xSPECT are considered to be statistical noise and a partial volume effect caused by low spatial resolution. All radioactive concentrations essentially converged within 48 iterations. The number of iterations recommended for the Siemens xSPECT is the same [26], but the mean radioactive concentrations for xQ and xB were similar at > 24 iterations. However, stable convergence was slightly delayed for F3D compared with
xSPECT, which has been explained by the study that compared OSEM and OSCGM [17]. The number of iterations is associated with a trade-off between signal and noise. Thus, we determined that 30 iterations were the most appropriate for xSPECT reconstruction in clinical practice. The FWHM with xQ and F3D considerably improved and converged at ~15 and 20 mm, respectively, when the number of iterations increased. Consequently, image quality was better for xQ at the appropriate parameter compared with F3D. In contrast, the spatial resolution in xB rarely changed even when the number of iterations increased, and the actual size of 10 mm was almost achieved. The xB iterative operation can be weighted by zero or any other value according to the corresponding zone class in the divided pixel [19]. Thus, we considered that not only bone class weighted by the optimal value, but also non-bone classes weighted by zero with a zonal map were responsible for the improved spatial resolution in the xB technology.

The xSPECT enhances SPECT images by applying the merit function to suppress noise caused by the fast convergence of OSCGM reconstruction. The Mighell-modified chi-squared gamma statistic algorithm is applied to the merit function for xSPECT reconstruction. Shinohara et al. found that Mighell-modified noise suppression was better than other image reconstructions based on chi-square statistics [32]. Thus, the xSPECT with the Mighell merit function considerably suppressed noise compared with F3D algorithms at the same number of iterations. Furthermore, xB suppressed image noise more effectively than xQ. Okuda et al. showed that the noise suppression effect differed between xQ and xB depending on the CT value [33]. In regions with low counts such as the background, the OSCGM based on the OSEM algorithm might lead to a contradictory effect of fast convergence. Background noise in xQ rapidly increased and appeared to differ from other images at 48 iterations (Fig. 4). An increasing CV with more iterations might have ramifications for lesion detectability. Therefore, we determined an appropriate number of iterations for clinical applications.

The RC with xSPECT which has high spatial resolution, was better than that of F3D due to the suppressed partial volume effect. However, the high spatial resolution of xB was not directly associated with an RC improved by the partial volume effect. This can be interpreted as being independent of the iterative operation of each zone class based on CT data, and the quantitative xB
image could be considered as a weighting effect of each tissue class that does not increase bone uptake.

Our clinical study showed that the quantitative indexes did not significantly differ (p > 0.05) between the xQ and xB algorithms, and in fact were equivalent. These findings were similar to the results of a previous phantom experiment [10]. Consequently, the spatial resolution was better in xB than xQ images and thus image quality was high and quantitative accuracy was equivalent. However, quantitative variation caused by misalignments such as motion and respiratory error during clinical scanning is a concern. In particular, xB imaging might cause different behavior due to the unique zone map system. Therefore, misalignment between SPECT and CT due to respiratory errors such as the ribs and sternum should be considered when clinically applying xB.

The present study has several limitations. Reconstructed SPECT images were assessed using different cross-calibration methods. The CCF on quantitative SPECT images varied depending on the radioactive concentration [34]. Thus, slight quantitative errors might arise between the F3D and xSPECT models. In addition, the body types of the 20 patients were essentially standard (average, 15.9 ± 2.8 MBq/kg). We could not take dependence on physique into consideration, and the impact of factors such as counts and scatter remains unclear. Further study is required to assess the relationship between body weight and the quality of images reconstructed using the xSPECT algorithm.

Conclusions

Bone images were qualitatively and quantitatively improved when reconstructed using OSGM-based xSPECT (xQ and xB) than OSEM-based F3D reconstruction. The xSPECT images using optimized reconstruction conditions were more sharply demarcated, with better quality, and lower background noise. One unique aspect of xB images is that the imaged content such as spatial resolution was independent of the number of iterations. Our findings provide important information that should facilitate understanding of the performance characteristics of the novel xQ and xB algorithms.

Abbreviations
xQ          xSPECT Quant
xB          xSPECT Bone
OSCGM       Ordered subset conjugate gradient minimizer
F3D         Flash 3D
FWHM        Full width at half maximum
CV          Coefficients of variance
RC          Recovery coefficients
SUV         Standardized uptake value
L4          4th vertebral body
BS          Bone scans
AC          Attenuation correction
SC          Scatter correction
SPECT/CT    Single-photon emission computed tomography/computed tomography
OSEM        Ordered subset expectation maximization
CCF         Cross-calibration factor
TBR         Tumor-to-normal bone ratios
ROI         Regions of interest

Declarations

Ethics approval and consent to participate

The Ethics Committee at the Cancer Institute Hospital of JFCR approved this clinical study (Approval no. 2015-1151). The results of this retrospective study did not influence further therapeutic decision-making.

Consent for publication

Not applicable

Availability of data and material

All data generated or analysed during this study are included in this published article
Competing interests
The authors declare that they have no competing interests

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Authors' contributions
NM contributed to the study design, phantom data acquisition and analysis of the data. KM and MO contributed to the study design, analysis of the data, and draft and critical revision of the manuscript. HI and AT contributed to the preparation of the study and critical revision of the manuscript. HI contributed to phantom data acquisition and interpretation. TT and MK contributed to the critical revision of the manuscript. All authors read and approved the final manuscript.

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Contributor Information
Noriaki Miyaji Email: noriaki.miyaji@gmail.com.
Kenta Miwa, Email: kenta5710@gmail.com.
Ayaka Tokiwa, Email: 1415079@g.iuhw.ac.jp.
Hajime Ichikawa, Email: ballocks10@yahoo.co.jp.
Takashi Terauchi, Email: takashi.terauchi@jfcr.or.jp.
Mitsuru Koizumi, Email: mitsuru@jfcr.or.jp.
Masahisa Onoguchi, Phone: +81-76-265-2526, Email: onoguchi@staff.kanazawa-u.ac.jp.

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Figures
Custom-designed phantom configured with vertebral body, spinous and transverse process, and a sphere set inside vertebral body to simulate bone metastasis.
Reconstruction plots show quantitative distribution in TBR1 (A), 2 (B), 4 (C) and 10 (D).

Filled and unfilled symbols indicate maximum and mean radioactive concentrations, respectively. Dotted line is actual radioactive concentration of phantom. Triangle - Flash 3D; Circle - xSPECT Quant; Square - xSPECT Bone.
Figure 3
Spatial resolution of three reconstructions at various iterations. Dotted line is actual size of phantom. Open triangle, Flash 3D (F3D); Open Circle, xSPECT Quant (xQ); Open Square, xSPECT Bone (xB).

Figure 4
Representative transaxial images of SPECT datasets including three reconstructions at TBR4. (A), Flash 3D (F3D); (B), xSPECT Quant (xQ); (C), xSPECT Bone (xB).
Figure 5

Coefficient of variance as a function of iteration numbers. Open triangle, Flash 3D (F3D); Open circle, xSPECT Quant (xQ); Open Square, xSPECT Bone (xB).
Recovery coefficients of three reconstructions at various numbers of iterations. Numbers of iterations in A, B, C, D, E, F, G and H are 12, 24, 36, 48, 60, 72, 84 and 96, respectively. Open triangle, Flash 3D (F3D); Open circle, xSPECT Quant (xQ); Open square, xSPECT Bone (xB).
Figure 7

Bar graphs of SUVmax and CV in xQ and xB. Unfilled and filled bars indicate xQ and xB, respectively.