Comparison between two super-resolution implementations in PET imaging

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(Received 12 November 2007; revised 5 February 2009; accepted for publication 6 February 2009; published 25 March 2009)

Super-resolution (SR) techniques are used in PET imaging to generate a high-resolution image by combining multiple low-resolution images that have been acquired from different points of view (POV). In this article, the authors propose a novel implementation of the SR technique whereby the required multiple low-resolution images are generated by shifting the reconstruction pixel grid during the image reconstruction process rather than being acquired from different POVs. The objective of this article is to compare the performances of the two SR implementations using theoretical and experimental studies. A mathematical framework is first provided to support the hypothesis that the two SR implementations have similar performance in current PET/CT scanners that use block detectors. Based on this framework, a simulation study, a point source study, and a NEMA/IEC phantom study were conducted to compare the performance of these two SR implementations with respect to contrast, resolution, noise, and SNR. For reference purposes, a comparison with a native reconstruction (NR) image using a high-resolution pixel grid was also performed. The mathematical framework showed that the two SR implementations are expected to achieve similar contrast and resolution but different noise contents. These results were confirmed by the simulation and experimental studies. The simulation study showed that the two SR implementations have an average contrast difference of 2.3%, while the point source study showed that their average differences in contrast and resolution were 0.5% and 1.2%, respectively. Comparisons between the SR and NR images for the point source study showed that the NR image exhibited averages of 30% and 8% lower contrast and resolution, respectively. The NEMA/IEC phantom study showed that the three images (two SR and NR) exhibited different noise structures. The SNR of the new SR implementation was, on average, 21.5% lower than the original implementation largely due to an increase in background noise, while the NR image had averages of 18.5% and 8% lower SNR and contrast, respectively, versus the two SR images. The new SR implementation can potentially replace the original SR approach in current PET scanners that use block detectors while maintaining similar contrast and resolution, but at a relatively lower SNR. A major advantage of the new SR implementation is its shorter overall scan duration which results in an increase in scanner throughput and a reduction in patient motion. © 2009 American Association of Physicists in Medicine. [DOI: [10.1118/1.3090890](https://doi.org/10.1118/1.3090890)]

Key words: super-resolution, PET imaging, image reconstruction, image resolution

I. INTRODUCTION

PET imaging with ^{18}F -FDG has been widely used to evaluate whether a tumor is benign or malignant.¹⁻³ The application of ^{18}F -FDG PET to characterize solitary pulmonary nodules (SPNs) has also been shown to be a highly sensitive and specific noninvasive diagnostic approach.^{4,5} Recent studies,^{5,6} however, have shown that SPNs of subcentimeter diameter are often missed mainly due to the poor resolution of PET images.

PET image resolution is affected by intrinsic and extrinsic factors. The intrinsic factors include detector size, positron range, and noncolinearity.⁷ Extrinsic factors, on the other

hand, include patient motion, reconstruction algorithms, and smoothing filters that further degrade the resolution of the resultant PET image. Many approaches have been proposed to overcome these effects.⁸⁻¹⁷ Some of these approaches relied on improving the intrinsic resolution of PET images by incorporating a model of the scanner point spread function during PET image reconstruction,⁸⁻¹⁰ while other approaches specifically focused on reducing the effects of the extrinsic factors such as gating the PET data acquisition to minimize motion.¹¹⁻¹⁴ Other techniques for improving PET image resolution have also explored the use of continuous bed motion to reduce the aliasing effects in the axial direction (Z-axis).¹⁵⁻¹⁷

Recently, super-resolution (SR) techniques have been used in PET imaging to generate a high-resolution image by combining multiple low-resolution images that have been acquired from different points of view (POV).^{18,19} Kennedy *et al.*¹⁸ applied SR techniques to PET imaging and demonstrated its impact on the quality of clinical PET images. In their implementation, however, the multiple images were acquired sequentially, each time by translating or rotating the same object by a subpixel distance with respect to the previous acquisition. The acquisition of multiple images from different POVs requires long scan duration, which ultimately leads to two main disadvantages of this approach, particularly when applied to patient studies. First, the increased scan duration reduces the scanner's throughput. Methods to decrease scan duration by shortening acquisition time results in images that are characterized by low signal-to-noise ratio (SNR), which ultimately obfuscates any improvement in image contrast and resolution. Second, long scan durations potentially increase the probability of patient motion. Any resolution improvement obtained through the application of the SR technique is compromised when patients move between POVs since such motion will lead to blurring of small objects in the resulting SR image.

In this paper, we propose a different implementation of the SR technique that does not suffer from these drawbacks. Rather than moving the same objects or patients to generate multiple images from different POVs, we propose to shift the image reconstruction pixel grid by the same amount to generate the required images. In this regard, the effects of long scan duration and patient motion will be minimized; furthermore, the resulting SR images will potentially be less blurred and hence will more accurately quantify the underlying state when compared to images generated using the original SR implementation. From here onward, the proposed SR implementation will be referred to as the “new” SR implementation, while the implementation of Kennedy *et al.*¹⁸ will be referred to as the “original” SR implementation.

The objective of this paper is to investigate whether the new SR implementation can generate PET images with similar quality to those generated from the original SR approach with respect to resolution, contrast, and SNR. The comparison is conducted using simulation and experimental studies. We expect that if the new SR implementation has similar performance to the original SR, then it can be easily applied in the clinic as a postprocessing task, which is virtual to the patient and technologist operating the PET/CT scanner. For reference purposes, the performance of the two SR techniques is also compared, in the experimental studies only, to that of a native reconstruction (NR) image generated using a high-resolution pixel grid (256×256). This paper is not intended to show that SR techniques (either new or original) can improve PET image resolution or that they are comparable to other approaches^{7–17} for improving image resolution, but rather to compare the performance of two SR implementations (original and new) as applied to transaxial PET imaging with respect to contrast, resolution, noise, and SNR.

To support our proposed new SR implementation, we first

FIG. 1. (a) The overall process of the SR approach, and (b) a simple model of PET imaging.

provide a mathematical framework showing that the two SR implementations have similar performance. We then verify these findings using simulation and experimental studies.

II. MATERIALS AND METHODS

II.A. Super-resolution algorithm in PET imaging

Both of the two SR implementations (original and new) rely on the same SR algorithm^{20,21} to generate the final SR image. This algorithm is the same as that described by Kennedy *et al.*^{18,19} in their original SR implementation and is a linear and shift-invariant technique. The algorithm is summarized as follows:

- (1) Multiple low-resolution images are acquired from different POVs.
- (2) These low-resolution images are up-sampled to a high matrix size (using bilinear interpolation), then mathematically shifted to a common reference frame, and averaged to generate an initial high-resolution guess.
- (3) The high-resolution guess is shifted to the reference frames of the initial POVs and down-sampled to a lower matrix size to synthetically generate low-resolution images, given the high-resolution guess.
- (4) The synthetically generated low-resolution images of step 3 are compared to the measured low-resolution images of step 1. Discrepancies are calculated.
- (5) The discrepancies for each POV in step 4 are again up-sampled (using bilinear interpolation), shifted to a common reference frame, averaged, and used to update the high-resolution guess.
- (6) Steps 3–5 are repeated until the discrepancies (its root-mean-square-error) are minimized or until a maximum number of iterations is reached.

II.B. Mathematical framework

A mathematical framework is provided to show that the new and original SR implementations have similar perfor-

FIG. 2. (a) Forward projection at angle θ , and (b) the CFT of the back-projection kernel.

mances. Figure 1(a) shows that the overall SR approach (original or new) is composed of two steps: (1) Generation of multiple low-resolution images and (2) application of the SR algorithm to these images in order to generate the final SR image. Since the second step (SR processing—Sec. II A) is a linear and shift-invariant process, it will have similar effects on either form of step 1. In this regard, the comparison of the two SR implementations is reduced to a comparison between the methods used to generate the input images defined in step 1. Using this analysis, the objective of the mathematical framework becomes focused on showing that the multiple images generated from either SR implementations (original or new) contain similar contrast and resolution information.

We use a 2D PET imaging model [Fig. 1(b)] to investigate the similarity between the multiple images that are generated for the two SR implementations. This model can be easily extended to 3D. In Fig. 1(b), the continuous imaged object $I(x, y)$ is first forward-projected into the sinogram $S(r, \theta)$ based on the Radon transform,²² where r and θ are the linear and angular variables, respectively. After data acquisition, $n(r, \theta)$ is added to the sinogram to represent quantum noise, which can be modeled as a Poisson distribution.²² The resultant noisy sinogram $[S(r, \theta) + n(r, \theta)]$ is then sampled and back projected into image space to generate a reconstructed image $J(x, y)$. The forward projection of the object at arbitrary angle θ is illustrated in Fig. 2, where θ is the angle between the x axis and x_θ axis. Using the x_θ - y_θ coordinate system, the object $I(x, y)$ can be written as $I(x_\theta, y_\theta)$, whose 2D continuous Fourier transform (CFT) is specified as $I(u_\theta, v_\theta)$, where u_θ and v_θ are the frequency variables corresponding to space variables x_θ and y_θ , respectively. After the forward projection at angle θ , the projection data $S_\theta(x_\theta)$ (sinogram at angle θ) are obtained. Due to the finite detector size of the PET scanners, this forward-projection process works first as projecting the object at a certain angle θ and then applying a 1D low-pass filter $H^{FP}(u_\theta)$ to the projection. According to the *projection-slice theorem*,²² the CFT of the projection data $S_\theta(u_\theta)$ and the 2D CFT of the object $I(u_\theta, v_\theta)$ are related by the equation

$$S_\theta(u_\theta) = H^{FP}(u_\theta)I(u_\theta, v_\theta)|_{v_\theta=0} + n(u_\theta), \quad (2.1)$$

where $I(u_\theta, v_\theta)|_{v_\theta=0}$ represents the value of $I(u_\theta, v_\theta)$ under the condition $v_\theta=0$, and $n(u_\theta)$ is the CFT of the additive noise term. The low-pass filter $H^{FP}(u_\theta)$ is also called the forward-projection kernel, which represents the detector response of the PET scanners. The projection data must be first sampled at a certain rate $u_{\theta0}$ before it can be stored into memory. In this case, the CFT of the sampled projection $S_\theta^S(u_\theta)$ becomes a shifted and replicated version of $S_\theta(u_\theta)$,

$$\begin{aligned} S_\theta^S(u_\theta) &= u_{\theta0} \sum_{m=-\infty}^{+\infty} S_\theta(u_\theta - mu_{\theta0}) \\ &= u_{\theta0} \sum_{m=-\infty}^{+\infty} [H^{FP}(u_\theta - mu_{\theta0}) \\ &\quad \times I(u_\theta - mu_{\theta0}, v_\theta)|_{v_\theta=0} + n(u_\theta - mu_{\theta0})]. \end{aligned} \quad (2.2)$$

Considering both the direct and the immediately adjacent detectors, the sampling interval is half the detector size in transaxial PET imaging, and therefore the sampling rate $u_{\theta0}$ equals to $2/d$, where d is the detector size.⁷

Following data acquisition or forward projection at each angle θ , the resultant projections or sinograms $S_\theta^S(u_\theta)$ are back projected into image space to generate the reconstructed image. This process, also called reconstruction, can be divided into two steps: (1) Back projecting the sampled sinogram into a continuous image and (2) sampling the reconstructed continuous image to obtain a digital image. Step 1 can be performed using a filtered back-projection (FBP) algorithm, where the projection at each θ will first be convolved with a 1D filter $H_\theta(r)$,²² whose frequency spectrum is shown in Fig. 2(b). In Fourier space, this convolution in step 1 is a multiplicative process,

$$\begin{aligned} J_\theta(u_\theta) &= H_\theta(u_\theta)S_\theta^S(u_\theta) \\ &= H_\theta(u_\theta) \cdot u_{\theta0} \sum_{m=-\infty}^{+\infty} S_\theta(u_\theta - mu_{\theta0}) \\ &= u_{\theta0}H_\theta(u_\theta) \sum_{m=-\infty}^{+\infty} [H^{FP}(u_\theta - mu_{\theta0}) \\ &\quad \times I(u_\theta - mu_{\theta0}, v_\theta)|_{v_\theta=0} + n(u_\theta - mu_{\theta0})], \end{aligned} \quad (2.3)$$

where $J_\theta(u_\theta)$ represents the CFT of the back-projection result at angle θ originating from $S_\theta^S(u_\theta)$. Note that on the right side of Eq. (2.3), the aliasing effects exist between $H_\theta(u_\theta)$ and each replicated branch of $S_\theta(u_\theta)$, which is represented by index m . However, since block detectors are used in modern PET systems, the detector response $H^{FP}(r)$ is usually modeled as a Gaussian blurring function with a full width at half maximum (FWHM) of the detector size d .^{23–28} In this case, under a sampling rate of $u_{\theta0}=2/d$, the total contribution of all the aliasing frequency components accounts for less than 1% of the total contribution of all the frequency components (refer to the Appendix). Therefore, the aliasing effects in Eq. (2.3) become negligible and the interaction between $H_\theta(u_\theta)$

and any replicated branch of $J_\theta(u_\theta)$ can be disregarded when $m \neq 0$ because $H_\theta(u_\theta)$ is band limited to the range $[-u_{\theta 0}/2, u_{\theta 0}/2]$ [Fig. 2(b)]. In this case, Eq. (2.3) can be reduced to

$$J_\theta(u_\theta) \approx u_{\theta 0} H_\theta(u_\theta) H^{\text{FP}}(u_\theta) I(u_\theta, v_\theta)|_{v_\theta=0} + u_{\theta 0} H_\theta(u_\theta) n(u_\theta). \quad (2.4)$$

In the original SR implementation, multiple data sets (projections or sinogram) are acquired during the forward projection (data acquisition) by moving the object. These objects in different locations are related to one another by a phase shift in their CFT,

$$I_k(u_\theta, v_\theta) = I(u_\theta, v_\theta) \exp[2\pi j(u_\theta \Delta x_{\theta k} + v_\theta \Delta y_{\theta k})], \quad (2.5)$$

$$k = 1, 2, 3, \dots, K,$$

where $\Delta x_{\theta k}$ and $\Delta y_{\theta k}$ represent the object movement along the x_θ and y_θ directions for the k th POV of the object, respectively. In the new SR implementation, however, only one data set is acquired during the forward projection. However, this only data set will be reconstructed in different POVs during the back projection (reconstruction) by shifting the reconstruction grid by the same amount as in the original SR implementation (the same $\Delta x_{\theta k}$ and $\Delta y_{\theta k}$). This reconstruction grid shift corresponds to a phase shift in the CFT of the back-projection kernel $H_\theta(r)$, according to the properties of convolution,²⁹

$$H_{\theta k}(u_\theta) = H_\theta(u_\theta) \exp[2\pi j(u_\theta \Delta x_{\theta k})], \quad k = 1, 2, 3, \dots, K. \quad (2.6)$$

When Eqs. (2.5) and (2.6) are plugged into Eq. (2.4), Eq. (2.4) becomes Eqs. (2.7) and (2.8) for the original and new SR implementations, respectively,

$$J_{\theta k}(u_\theta) \approx u_{\theta 0} H_\theta(u_\theta) H^{\text{FP}}(u_\theta) I(u_\theta, v_\theta)|_{v_\theta=0} \exp(2\pi j u_\theta \Delta x_{\theta k}) + u_{\theta 0} H_\theta(u_\theta) n_k(u_\theta), \quad (2.7)$$

$$J_{\theta k}(u_\theta) \approx u_{\theta 0} H_\theta(u_\theta) H^{\text{FP}}(u_\theta) I(u_\theta, v_\theta)|_{v_\theta=0} \exp(2\pi j u_\theta \Delta x_{\theta k}) + u_{\theta 0} H_\theta(u_\theta) n(u_\theta) \exp(2\pi j u_\theta \Delta x_{\theta k}). \quad (2.8)$$

The above analysis [Eqs. (2.1)–(2.8)] holds for all possible angles θ , although they have different x_θ , y_θ , u_θ , v_θ , Δx_θ , Δy_θ , and $H_\theta(r)$. Therefore, the results from all these angles θ will be summed to generate the final image.

$$J_k(u, v) = \sum_{\text{all } \theta} J_{\theta k}(u_\theta). \quad (2.9)$$

This final back-projection result is still a continuous reconstructed image and has to be sampled at certain rates u_0 and v_0 in the X and Y directions before display. The CFT of the final digital image becomes a shifted and replicated version of $J_k(u, v)$,

$$J_k^S(u, v) = u_0 v_0 \sum_{m=-\infty}^{+\infty} \sum_{n=-\infty}^{+\infty} J_k(u - m u_0, v - n v_0). \quad (2.10)$$

Comparison between Eqs. (2.7) and (2.8) shows that the multiple images that are generated using either the original or the new SR implementation have the same contrast and resolution information (first term) but different noise contents (second term). In the original SR implementation, the noise content comes from different data acquisitions which are independent of one another. In the new SR implementation, however, the noise content arises from the same data acquisition process and hence the noise-related terms are strongly coupled to one another by phase shifts in their frequency responses. Therefore, the proposed new SR implementation is expected to generate PET images with similar contrast and resolution but different noise contents (frequencies and amplitude) as the original SR implementation.

The above mathematical analysis also suggests that the frequency response of the final SR images generated using either the original or the new SR implementation are both affected by the band-limited properties of the detector response $H^{\text{FP}}(u_\theta)$. Therefore, when either SR processing is applied in transaxial PET imaging, no frequency component will be recovered that is above the cutoff frequency of the low-pass filter $H^{\text{FP}}(u_\theta)$, which is also determined by the detector size or the intrinsic resolution of the PET scanner. In other words, SR processing cannot generate a PET image that is above the intrinsic resolution.

It is important to note that the mathematical analysis conducted in this section is based on a linear shift-invariant model (FBP reconstruction). The same conclusion cannot be directly extended to nonlinear statistical reconstructions, such as OSEM. In this regard, our simulation and experimental studies were conducted using FBP. However, since the current standard of PET image reconstruction is based on nonlinear statistical approaches, we have also performed the simulation and experimental studies using OSEM reconstruction.

II.C. Simulation study

Based on the mathematical framework, a simulation study was conducted to evaluate the equivalence between the original and the new SR implementations. This evaluation was performed for both FBP and OSEM reconstructions of the multiple low-resolution images. The simulation code was written using MATLAB in a PC environment. The reconstruction algorithms (FBP and OSEM) used in this section were based on *Fessler's Image Reconstruction Toolbox*.³⁰

In this study, a digital phantom ($36 \times 36 \text{ cm}^2$) containing spheres of different diameters (32, 25, 18, 7.2, and 3.6 mm, respectively) was simulated and positioned at the center of the FOV of the scanner (Fig. 3). The sphere-to-background ratio (SBR) was set to 5:1 and all data were acquired in 2D mode. The digital phantom was then forward projected into sinogram space and Poisson noise was added. The resultant sinograms were then reconstructed in a FOV of 46 cm using both FBP and OSEM (2 iterations and 21 subsets). To generate a SR image using the original implementation, four low-resolution images (matrix size: 128×128 ; pixel size: 3.6 mm) were reconstructed from four different data sets (sino-

FIG. 3. Configuration of the simulation study: PET scanner and digital phantom.

gram) that were acquired from four different POVs. The centers of the four different POVs formed a 2×2 square lattice with each POV centered at (0, 0), (0, 1.8), (1.8, 1.8), and (1.8, 0) mm, respectively. The original SR image (matrix size: 256×256 ; pixel size: 1.8 mm) was then generated by combining these four low-resolution images using the SR algorithm (Sec. II A). In addition, the new SR image was generated by combining four low-resolution images which were reconstructed from four different POVs of the *first* data set only. The multiple POVs associated with the new SR implementation were realized by shifting the reconstruction grid by the same amount as in the original SR implementation. The original and new SR images were generated for both FBP and OSEM reconstructions of the multiple low-resolution images. The resultant SR images (original and new) were then compared with each other using line profiles drawn across the 7.2 and 3.6 mm spheres, and their corresponding contrast ratios (CRs) were calculated. Since we simulated multiple (seven) 7.2 and 3.6 mm spheres, the CR in this case was defined as

$$CR = \frac{\frac{1}{7} \sum_{i=1}^7 P_i - \frac{1}{6} \sum_{j=1}^6 T_j}{\frac{1}{7} \sum_{i=1}^7 P_i}, \quad (2.11)$$

where P_i represents the amplitude of the i th peak, while T_j represents the amplitude of the j th valley (trough) across the line profile of the seven 7.2 or 3.6 mm spheres.

In addition, SNRs of the different spheres were plotted and compared between the two SR images. The SNR was determined by calculating the ratio between the average pixel value inside each sphere and the noise level. The noise

FIG. 4. The setup of the point source study. Two point sources were placed at (1) $X = -3$ cm, $Y = 0$ cm, and (2) $X = 4$ cm, $Y = 0$ cm in the FOV of the PET scanner.

in this case was calculated based on the standard deviation of 60 randomly selected pixels in the phantom background.

The same evaluation as above was repeated for three different PET scanners having different numbers of detectors per ring (400, 600, and 1000) but with the same FOV size. Since the PET scanner simulated in this study has a FOV of 70 cm, the numbers of detectors (400, 600, and 1000) correspond to scanner detector sizes of 5.5, 3.7, and 2.2 mm, respectively. These detector sizes are similar to those in current commercial PET scanners. Consequently, by comparing the results from the different scanners, the effects of the scanner's detector size on SR processing (original and new) can be demonstrated. All the simulations for the three PET scanners were repeated 50 times. The contrast ratios and background noise levels were determined and listed, and SNRs versus different sphere sizes were plotted for both the original and new SR implementation for each scanner, and for both the FBP and the OSEM reconstructions.

II.D. Experimental phantom studies

II.D.1. PET data acquisition

Experimental data for the point source and NEMA/IEC phantom studies were acquired on a DISCOVERY RX PET/CT scanner (GE Healthcare, Waukesha, Wisconsin). The gantry of this PET scanner consists of 24 rings of 630 detector crystals per ring. The detector material of this scan-

FIG. 5. The setup of the NEMA/IEC phantom study.

Simulation Study (FBP)

FIG. 6. The results from the simulation study using FBP reconstructions. The line profiles across 3.6 mm spheres of the two SR images for the three scanners (400, 600, and 1000 detectors) are shown in (a)–(c), respectively. The SNR comparisons between the two SR images for the three scanners are shown in (d)–(f), respectively.

ner is LYSO. The PET scanner has a transaxial FOV of 70 cm and a 15.7 cm axial extent. PET data can be acquired in both 2D and 3D modes and can be reconstructed using any of three matrix sizes: (1) 64×64 , (2) 128×128 , and (3) 256×256 . The description and performance characteristics of this scanner have been published elsewhere.²⁸ The reconstruction FOV of this scanner can be changed in increments of 0.1 mm and shifted along the *X* (left-right) and *Y* (up-down) axes in increment of 0.1 mm. All acquired data were corrected for attenuation, scatter, and dead time and reconstructed using FBP (with ramp filter) and OSEM (2 iterations and 21 subsets) algorithm. The FBP and OSEM reconstruction algorithms as implemented on the GE system do not include any compensation for detector response.

II.D.2. Point source study

The mathematical framework in Sec. II B suggested that the two SR implementations (original and new) are expected to result in similar image contrast and resolution in current PET scanners that use block detector designs. To validate

this finding, a point source study was specifically designed to investigate this result using a commercially available PET scanner.

The point source was made by pipetting a 1 μ l drop of ^{18}F -FDG having a concentration of 10 MBq/cm³ onto a glass slide. The radioactive drop was then pulled into a hematocrit capillary tube (Fisher Brand glass heparinized microhematocrit capillary tube, Pittsburg, PA) by capillary action to form a point source of activity. Two such sources were made and attached to a plastic stick that was mounted on a motor-controlled platform.³¹ The positions of the two point sources were at $(-3, 0)$ and $(4, 0)$ cm from the center of the scanner, as shown in Fig. 4.

The two point sources were imaged 16 times in 2D mode, each for a total of 5000 kg counts. The same number of counts was used each time to compensate for radioactive decay. Following each data acquisition, the two point sources were shifted by 1 mm along either the *X* axis or the *Y* axis with respect to the previous acquisition. The *Y*-axis shift was achieved by adjusting the position of the patient couch (tolerance of the patient couch is 0.5 mm), while the *X*-axis shift

Simulation Study (OSEM)

FIG. 7. The results from the simulation study using OSEM reconstructions. The line profiles across 3.6 mm spheres of the two SR images for the three scanners (400, 600, and 1000 detectors) are shown in (a)–(c), respectively. The SNR comparisons between the two SR images for the three scanners are shown in (d)–(f), respectively.

was realized by changing the position of the motor-controlled platform. Using this acquisition paradigm, the centers of the 16 different POVs formed a 4×4 square lattice, with each two locations separated by 1 mm with respect to one another. The center of the first acquisition was at position (0, 0). Following data acquisition, a low-resolution image was first reconstructed using a matrix size of 64×64 in a FOV of 25.6 cm from each of the 16 data acquisitions. In addition, another group of 16 low-resolution images using the same matrix size and FOV as before was also reconstructed from the first data set [position (0, 0)] by shifting the reconstruction pixel grid each time by 1 mm along either the X or Y axes to generate a corresponding 4×4 square lattice. In both cases, the 16 low-resolution images were then combined with one another according to the SR algorithm (Sec. II A above) to generate the original and new SR image (256×256), respectively. The above image reconstructions and SR processing were conducted for both FBP (with ramp filter) and OSEM (2 iterations, 21 subsets, with no smoothing) algorithm. For comparison purposes, a 256×256 NR image was also directly reconstructed from the first data set

in the same FOV using OSEM (2 iterations, 21 subsets, with no smoothing). The two SR images from either the FBP or OSEM reconstruction were then compared to each other using visual inspection and line profiles. In addition, the peak amplitude and the FWHM for each point source in the five images [original SR (FBP and OSEM), new SR (FBP and OSEM) and NR] were determined to measure the contrast ratio and image resolution, respectively.

II.D.3. NEMA/IEC phantom study

The mathematical framework in Sec. II B suggested that the two SR implementations are expected to differ only in their noise content. In this regard, the NEMA/IEC phantom study was designed to compare the noise properties and SNRs of the two SR implementations in a pseudoclinical environment.

A NEMA/IEC phantom containing six spheres of different sizes (diameter: 10, 13, 17, 22, 28, and 37 mm) and a hollow insert (cylinder with a diameter of 51 mm) was filled with ^{18}F -FDG water using a SBR of 10.5:1. The phantom was

positioned on a motor-controlled platform similar to the one used in the point source study. A lead block was used to counter balance the weight of the NEMA/IEC phantom (Fig. 5). The whole system (phantom, lead block, and the motor-controlled platform) was positioned at the center of the FOV of the PET scanner (Fig. 5) and data were acquired in 2D mode. Sixteen different data sets were acquired by moving the NEMA/IEC phantom along the X axis or the Y axis in 2 mm steps. Each acquisition contained 4900 kg counts. The positions of the phantom in these 16 data acquisitions formed a 4×4 square lattice. Following data acquisition, a low-resolution image with a matrix size of 64×64 was reconstructed in a FOV of 51.2 cm from each of the 16 acquired data sets, respectively. In addition, another group of 16 low-resolution images using the same matrix size and FOV as before was reconstructed from the first data set by shifting the reconstruction pixel grid each time by 2 mm along either the X or Y axes to generate a corresponding 4×4 square lattice. In both cases, the 16 low-resolution images were then combined with one another according to the SR algorithm (Sec. II A above) to generate the original and new SR images (256×256), respectively. In both cases, the reconstruction was performed using FBP and OSEM. For comparison purposes, a 256×256 NR image was also directly reconstructed from the first data set in the same FOV using OSEM (2 iterations and 21 subsets). A 4.5 mm Gaussian postfilter was used during this reconstruction to equalize the background noise between the new SR and the NR images.

For the two SR images and the NR image, the noise level was first evaluated using visual inspection and then measured by calculating the standard deviation of 60 randomly selected pixels in the background. This process was repeated 20 times using different axial slices, and the mean and standard deviation of the noise level were determined to represent the background noise of the phantom. In addition, a region of interest (ROI) was drawn on each sphere based on CT images. The signal value was then calculated as the average of all the pixels inside each ROI, and SNRs for each sphere were calculated as the ratio between the signal values and background noise of the phantom. Furthermore, a 31×31 square ROI was drawn in the background of each image, and a 2D Fourier transform (FT) was applied in order to investigate the difference in noise structure among the four SR images and the NR image. A line profile along each sphere was also drawn in the three images to compare their contrast properties. All the comparisons between the original and new SR images were conducted for both the FBP and the OSEM reconstructed images.

III. RESULTS

III.A. Results from the simulation study

The line profiles across the 3.6 mm spheres of the two SR images (original and new) reconstructed using FBP are shown in Figs. 6(a)–6(c) for PET scanners with 400, 600, and 1000 detectors, respectively. The corresponding results for OSEM reconstructions are shown in Figs. 7(a)–7(c). In all figures, the dotted and solid lines correspond to the per-

TABLE I. Simulation study (N/R—not resolved).

Scanner	FBP		OSEM	
	Original SR	New SR	Original SR	New SR
(A) Contrast ratio across 7.2 mm spheres in simulation study				
400 detector	0.28 ± 0.03	0.31 ± 0.05	0.75 ± 0.02	0.72 ± 0.04
600 detector	0.73 ± 0.03	0.72 ± 0.03	0.77 ± 0.02	0.77 ± 0.03
1000 detector	0.87 ± 0.03	0.86 ± 0.03	0.78 ± 0.01	0.78 ± 0.01
(B) Contrast ratio across 3.6 mm spheres in simulation study				
400 detector	N/R	N/R	0.32 ± 0.06	0.31 ± 0.08
600 detector	N/R	N/R	0.48 ± 0.05	0.48 ± 0.06
1000 detector	0.74 ± 0.03	0.73 ± 0.05	0.58 ± 0.04	0.57 ± 0.04
(C) Background noise in simulation study (Bq/cm ³)				
400 detector	425 ± 19	557 ± 34	583 ± 20	699 ± 36
600 detector	534 ± 24	614 ± 32	475 ± 25	563 ± 21
1000 detector	865 ± 50	954 ± 38	303 ± 14	349 ± 17

formance of the new and original SR images, respectively. These line profiles suggest that the two SR images (original and new) have similar performance. The same results can be observed for OSEM reconstruction. The contrast ratios for the 7.2 and 3.6 mm spheres are summarized in Tables I, respectively, for each scanner, SR approach (original and new) and reconstruction algorithm (FBP and OSEM). This table indicates that the contrast difference between the two SR images is always less than 10% (average of 2.3%) independent of scanner design and reconstruction algorithm of the multiple low-resolution images. Tables I also show that the contrast ratio for both SR images increases as the number of detectors increases, suggesting that higher contrast ratio can be achieved by improving the intrinsic resolution of the PET detectors.

The SNR plots for each sphere and scanner design are shown in Figs. 6(d)–6(f) for FBP reconstruction and in Figs. 7(d)–7(f) for OSEM reconstruction. Here also, the dotted and solid lines represent the SNR curve for the new and original SR images, respectively. The phantom background noise levels were also listed in Table I for the two SR images and three scanner types and for both FBP and OSEM reconstructions. These noise levels, as well as the SNR plots, suggest that the new SR image always has a higher background noise (average of 18.3% higher) and lower SNR (average of 14.9% lower) when compared to the original SR image. These results as well as that from the line profiles suggest that although the two SR images have similar contrast, they however, contain different noise contents, which supports the conclusions of the mathematical framework.

III.B. Results from experimental phantom studies

III.B.1. Point source study

The results of the point source study for the original and new SR implementations using FBP and OSEM are shown in Figs. 8(a)–8(d), while the 256×256 NR image is shown in Fig. 8(e). Point source II had similar results as point source I

Point Source Study

FIG. 8. The results from the point source study: Image of point source I for (a) original SR (FBP), (b) new SR (FBP), (c) original SR (OSEM), (d) new SR (OSEM), and (e) NR image. The radial and tangential line profiles for the five images are shown in (f) and (g), respectively.

and hence is not included in this figure. All images were normalized to the same color scale. The corresponding radial and tangential line profiles across the five images are also shown in Figs. 8(f) and 8(g), respectively. The results of the peak amplitudes and FWHMs of the two point sources in the five images [original SR (FBP and OSEM), new SR (FBP and OSEM), and NR] are summarized in Tables II, respectively. The peak amplitudes in Table II are normalized to the original SR image, for both the FBP (original and new SR) and OSEM (original SR, new SR, and NR) reconstructions.

From visual inspection, the two point sources in the new SR image are similar to those of the original SR image. Line profiles in Figs. 8(e) and 8(f) show that the new and original SR images exhibit the same signal amplitude and FWHM for both the FBP and OSEM reconstructions, respectively. These results are also confirmed in Tables II. Table II shows that the two SR images have an average difference of 0.5% in peak amplitude, which indicates that the two SR implementations can achieve the same contrast. Table II shows that the two SR images have average differences of 1.3% and 1.1% in FWHM for the FBP and OSEM reconstructions, respectively, which suggests that the two SR implementations have simi-

lar resolution performance. These results confirmed the conclusion of the mathematical framework that the two SR implementations can achieve similar image resolution and contrast ratios. For comparison, the 256×256 NR image only reaches an average of 70% of the signal amplitude and has an 8% wider FWHM when compared to the two SR (original and new) images which are generated using OSEM reconstructions.

III.B.2. NEMA/IEC phantom study

The SR images of the NEMA/IEC phantom which were generated from the original and new implementations using FBP and OSEM are shown in Figs. 9(a)–9(d), while the 256×256 NR image is shown in Fig. 9(e). All images are displayed with the same color scale. Using visual inspection, all spheres can be resolved in all five images; however, the noise structure in these images is clearly different. In the original SR images, the noise is relatively smooth, whereas in the new SR images it is “clumpy,” while in the NR image it is “pixilated.”

TABLE II. Point source study.

(A) Peak amplitudes for the two point sources				
Peak amplitude (normalized to original SR)	Point source I		Point source II	
Original SR (FBP)	1		1	
New SR (FBP)	0.99		0.99	
Original SR (OSEM)	1		1	
New SR (OSEM)	1		0.99	
NR (OSEM)	0.69		0.71	

(B) FWHM for the two point sources (mm)				
	Point source I		Point source II	
	Radial	Tangential	Radial	Tangential
Original SR (FBP)	6.0	5.8	5.9	5.9
New SR (FBP)	5.9	6.0	5.9	5.9
Original SR (OSEM)	4.5	4.5	4.5	4.4
New SR (OSEM)	4.5	4.6	4.5	4.5
NR (OSEM)	4.9	4.8	5.0	4.8

Noise spectra (2D FT) derived from a square ROI drawn in the background of the five images are shown in Figs. 9(f)–9(j), respectively. The average ROI pixel value was subtracted from each pixel in the spectrum analysis to suppress the DC component (frequency is 0). The noise spectra in Figs. 9(f)–9(i) clearly show that the amplitude (intensity) of low frequency components is higher in the new SR image when compared to the original SR image. This observation is reversed for the high frequency components. In other words, the noise in the original SR image is more “white” versus the new SR image. The same observation was found for both FBP and OSEM reconstructed images. Figure 9(j), however, showed that although the NR image was reconstructed to have the same noise level as the new SR image, it has a wider frequency range in its noise spectrum versus the new SR image.

A quantitative assessment of the noise level in the phantom background of the four images is shown in Table III. These results indicate that the background noises of the original SR image are 23.6% and 18.2% lower than the new SR image using FBP and OSEM reconstructions, respectively. The table also confirms that the background noise in the NR image is similar to that in the new SR image. A quantitative comparison of the sphere SNR among the four SR images and the NR image is shown in Fig. 9(k). This figure shows that the two SR images (original and new) have average differences over all six spheres of 24.2% and 18.8% in SNR for the FBP and OSEM reconstructions, respectively. For comparison, the 256×256 NR image has averages of 28.6% and 8.4% lower SNR versus the original and new SR images, respectively. The decrease in SNR with sphere size for all five images is mainly due to partial volume effect.

Figure 9(l) shows the line profile across the 10 mm sphere for all five images. This line profile shows that the two SR images have similar contrast (average of 5% difference) since they have line profiles with similar maximum and minimum pixel values. This observation was the same for

both FBP and OSEM reconstructed images. This figure also shows that the contrast of the NR image is slightly worse (average of 8%) than the two SR images.

IV. DISCUSSION

In this paper, we demonstrated the feasibility of implementing a new SR technique by combining multiple low-resolution images from different POVs generated by shifting the reconstruction pixel grid rather than moving the objects or patients. The results of our mathematical framework showed that from a theoretical standpoint, the new SR implementation was expected to have similar performance but different noise contents when compared to the original SR implementation in current PET scanners that use block detectors. Based on these findings, the new SR implementation was compared to the original SR approach using simulation and experimental phantom studies. For reference purposes, a comparison with a NR image using a high-resolution pixel grid was also performed. The results of these studies supported the mathematical framework by showing that the two SR implementations have similar contrast and resolution but relatively different SNRs. Furthermore, these results were shown to be similar, independent of the reconstruction algorithm used (FBP or OSEM). The results also showed that the two SR approaches had better performance in image quality than the NR image. In this regard, the new SR implementation can replace the original implementation with minimal impact on the image quality. An added advantage of the new SR implementation is its shorter scan duration (since only one data acquisition is required). Shorter scan duration increases scanner throughput and minimizes the potential of patient motion, thereby improving the quality of the resulting SR images. In addition, the new SR approach is purely a postprocessing technique not requiring any user interaction and can be implemented in a similar manner to current image reconstruction tasks.

NEMA/IEC Phantom Study

FIG. 9. Images of the NEMA/IEC phantom study for (a) original SR (FBP), (b) new SR (FBP), (c) original SR (OSEM), (d) new SR (OSEM), and (e) NR image. The noise spectra in the corresponding black squares are shown in (f)–(j), respectively. The SNR vs different sphere diameters for different SR approaches and reconstruction algorithms as well as the NR image are shown in (k). Line profiles across the 10 mm sphere for the five images are shown in (l).

Intuitively one would expect the original SR implementation to generate images with superior resolution since they were created from multiple data sets rather than a single acquisition as in the case of the proposed SR implementation. However, our mathematical framework as well as our simulation and experimental results showed otherwise. The main reason for this observation is that the transaxial PET images have already been sufficiently sampled from a Nyquist perspective primarily due to the band-limited properties of the PET detector response. Therefore, the multiple

data sets in the original SR implementation do not provide any additional resolution information or spatial frequencies but rather only additional noise realizations with similar spatial content, albeit sampled from different POVs. In such scenarios, the sampling is improved but the spatial frequency content is the same due to the band-limited properties (or intrinsic resolution) of PET scanner detectors. The same rationale also applies to the new SR implementation. This results in similar image resolution for either implementation, as was shown in the point source study. The ability to improve PET image resolution using SR techniques (original and new), however, is always limited by the intrinsic resolution of the PET detectors, as was shown in the comparisons among the three PET scanners in the simulation study. In other words, SR techniques (original and new) can only be used in transaxial PET imaging to recover resolution degradation due to the existence of the extrinsic factors that affect PET image resolution. Improvement beyond the intrinsic resolution of PET detectors, however, can be achieved, for ex-

TABLE III. NEMA/IEC phantom study (N/A—not applicable).

Background Noise for NEMA/IEC phantom study			
Noise (Bq/cm ³)	Original SR	New SR	NR
FBP	1557 ± 434	2038 ± 257	N/A
OSEM	505 ± 87	617 ± 91	626 ± 97

FIG. 10. (a) Contrast vs noise curves for the original SR (OSEM, dashed line), new SR (OSEM, dotted line), and NR (solid line) for the NEMA/IEC phantom study. (b) The SNR in the NEMA/IEC phantom study versus iterations of the SR algorithm for spheres of 37, 28, 22, and 17 mm diameters.

ample, by modeling the detector response during image reconstruction as demonstrated by Panin *et al.*¹⁰ as well as others.

To perform an unbiased comparison between the SR and the NR images, the parameters of the NR OSEM reconstruction were chosen to equalize the background noise between the new SR and the NR images. Under these conditions, the original and new SR images exhibited higher SNR and contrast compared to the NR image, suggesting that they have better image quality. To gain a better understanding of the improvement in image quality of the SR images, we plotted the contrast versus noise curves of the original SR (OSEM), new SR (OSEM), and NR images for the 10 mm sphere in the NEMA/IEC phantom in Fig. 10(a). Different noise levels were generated by applying different filter FWHM (0.1–20 mm) to the three images. Contrast was defined as the difference in the average pixel values in the 10 mm sphere and a background ROI divided by the average pixel value in the sphere. The comparison among the three curves suggests that for the same background noise, the two SR images always have higher contrasts than the NR image, thereby achieving better SNR. These results supported our finding in the point source study that the two SR implementations can generate PET images that have a higher spatial resolution (narrower FWHM) versus the NR reconstruction [Table II] primarily due to the fact that SR techniques can improve PET image contrast. We believe that the reason why SR techniques can achieve better contrasts versus the NR reconstruction is because SR images were generated from image reconstructions using a coarser grid while the NR images are directly reconstructed using a finer grid. The reconstruction using a finer grid results in relatively lower radioactive counts per image pixel, therefore resulting in nonconvergence for the chosen number of iterations and subsets under the condition of equalized background noise.

In common with many image reconstruction algorithms,

the SR approach is iterative in nature, and hence, the number of iterations utilized has the potential of greatly impacting the final results. During SR processing, the average discrepancy between the high-resolution guess and the up-sampled image in each POV is added to the high-resolution guess before updating each iteration (SR algorithm—Sec. II A above). The criteria for stopping are either that the discrepancy is minimized or a maximum number of iterations are reached. The maximum number of iterations used in this paper was 20 for both the original and new SR implementation. Increasing the number of iterations increases the contrast but also increases at a faster rate the noise content in the final image. The net effect results in an image with a lower SNR, as shown in Fig. 10(b). This figure plots the SNR versus different numbers of SR iterations for four different sphere sizes.

One limitation of this paper is that the background noise level in the NEMA/IEC phantom study was evaluated based on only one data set, albeit using multiple PET slices rather than multiple phantom scans. A more suitable noise evaluation would be based on statistical results from multiple data acquisitions that have the same experimental environment (SBR, count density, etc). This requirement, however, is difficult to achieve in experimental phantom studies due to its heavy workload. To overcome this difficulty, we performed our noise evaluation in the simulation studies based on multiple data acquisitions (50 noise realizations). These results showed that the variation in background noise (std/mean) between the two SR implementations was 4%. Based on these results, we expect that the phantom results using a single data acquisition to represent a valid approximation of the true noise variation.

Another limitation of this paper is that comparison between the two SR implementations in patient studies was not performed. This is mainly due to the difficulty in implementing the original SR technique in patient scans. To realize the

original SR image, patients must be scanned for longer duration to acquire multiple data sets from different POVs. This long scanning duration will lead to patient discomfort and potential motion. Furthermore, subpixel shifts are very difficult to realize in patient studies versus phantom studies since any patient motion (respiration, cough, or other random motions) during each data acquisition or between two different POVs will trade-off the resolution improvement from the application of the SR techniques.

The SR techniques come at the cost of increased computer processing time. We estimate that the new SR implementation would require about 15 times the processing time of the standard FBP or OSEM reconstruction when using 20 iterations for the SR algorithm. This estimation takes into consideration not only the faster reconstruction time needed for the lower resolution images necessary for SR image generation but also the increased time due to the multiple iterations required for SR convergence. The additional computation time, however, can be largely reduced if a smaller number of iterations is used. Furthermore, any future increases in computer processing speeds will further reduce these time limitations.

V. CONCLUSION

In this paper, we present a new implementation of the SR technique by combining multiple low-resolution images from different POVs which are realized by shifting the reconstruction pixel grid. This new SR implementation is compared to the original SR implementation using a mathematical framework, a simulation study, and experimental phantom studies. For reference purposes, a comparison with a NR image using a high-resolution pixel grid was also performed. The results from these studies show that the new SR implementation has similar image contrast and resolution but achieves slightly lower SNR in current PET scanners that use block detectors. In this regard, the new SR implementation can potentially replace the original SR implementation. A major advantage of the new SR implementation is shorter scan duration and consequent increase in scanner throughput and reduction of patient movement.

APPENDIX: ALIASING FREQUENCY COMPONENTS IN PET SCANNERS WITH BLOCK DETECTOR DESIGN

The detector response function $f(x)$ of the PET scanner in the transaxial direction can be written as a normalized Gaussian distribution with zero mean

$$f(x) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{x^2}{2\sigma^2}\right) \quad (\text{A1})$$

where σ is the standard deviation and x is the space coordinate variable. Modern PET/CT scanners usually use block detectors, whose response function can be modeled as a Gaussian function with a FWHM equal to the detector size d .^{24–29} Therefore,

$$f(d/2) = \frac{1}{2}f(0). \quad (\text{A2})$$

When Eq. (A1) is plugged into Eq. (A2), we obtain the relationship between the parameter σ and the detector size d ,

$$\sigma^2 = d^2/8 \ln 2. \quad (\text{A3})$$

When Eq. (A3) is plugged into Eq. (A1), Eq. (A1) becomes

$$f(x) = (4 \ln 2/\pi d^2)^{1/2} \exp(-4 \ln 2 \cdot x^2/d^2). \quad (\text{A4})$$

The FT of this function is also a Gaussian function,

$$F_x[f(x)](u) = \exp(-\pi^2 d^2 u^2/4 \ln 2). \quad (\text{A5})$$

Considering both the direct and the immediately adjacent detectors, the sampling interval per projection is usually set to half the detector size in transaxial PET imaging, and therefore the sampling rate u_0 equals to $2/d$,

$$u_0 = 2/d. \quad (\text{A6})$$

Using this sampling rate, the Nyquist frequency, which is the highest frequency that can be sufficiently represented, equals half of u_0 ; therefore,

$$u_N = u_0/2 = 1/d. \quad (\text{A7})$$

Any frequency component that is above u_N will thus be aliased. The total contribution of all the aliasing frequencies in this Gaussian detector response can be calculated by

$$\begin{aligned} C_A &= \frac{\int_{u_N}^{+\infty} F_x[f(x)](u) du}{\int_0^{+\infty} F_x[f(x)](u) du} \times 100\% \\ &= \frac{\text{erf}(+\infty) - \text{erf}(\pi/2 \sqrt{\ln 2})}{\text{erf}(+\infty)} \times 100\% \\ &= 0.76\%, \end{aligned} \quad (\text{A8})$$

where $\text{erf}(\cdot)$ is the error function. This assessment is based on the assumption that the object being imaged has a uniformly distributed frequency components. However, the frequency spectrum of the phantoms used in the experimental studies of this paper (as well as any patient study) is dominated by low frequencies, thereby further reducing the value of C_A and hence rendering the contributions of the aliasing frequencies to be further diminished ($\ll 1\%$).

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