A Scatter Calibration Technique for Dynamic Brain Imaging in High Resolution PET

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Abstract—We describe a scatter calibration technique which improves the quantitative accuracy of the positron emission tomography data in specific scanning conditions; i.e., scans with high random fraction (RF) and/or low number of counts. Such a situation is often encountered in dynamic imaging on scanners with a large number of lines-of-response (LOR) such as the high resolution research tomograph (HRRT). In this paper, we first describe how high RFs and low number of counts affect the scatter scaling process. We then demonstrate experimentally, with phantom studies, the bias in the scatter estimate introduced by the commonly used tail-fitting technique employed in the single scatter simulation (SSS) method. A significant bias in scatter fraction (SF) was found for frames which contain a RF higher than 50% and/or with a number of counts less than 20 M. Finally, we present a new scatter scaling technique which compensates this bias. The scatter calibration technique is based on using the scatter estimate obtained from a reference frame, in which the bias due to high RFs and low number of counts is minimized, to calibrate the scatter in each dynamic frame. The calibration also separately accounts for the change in SF due to the pulse pile-up effect. A much more consistent and accurate SF value was assigned to each segment of the scatter sinogram thus leading to a more quantitative reconstructed image with a better axial uniformity after the scatter calibration. The new calibration technique was tested with phantom, monkey, and human data and was found to significantly improve the quantitative aspect of the early frames: such improvement is expected to positively affect the feasibility of rather novel image analysis methods, such as determination of image derived input function.

Index Terms—PET data quantification and correction methods, PET reconstruction.

I. INTRODUCTION

SCATTER correction is a critically important and at the same time challenging step in the task of quantitative PET imaging. This is particularly the case in 3D PET in which the scatter fraction (SF) is typically as high as 30%–50%. The widely used scatter estimation process for 3D PET based on the single scatter simulation (SSS) [1], [2] generally consists of two parts: one is to obtain the spatial scatter distribution within the object, and the other is to scale the magnitude of that distribution to account for scatter originating from outside the field of view (FOV) and to make it commensurate with the measured coincidences. The scaling process incorporates the observation that since there should be no activity outside the boundary of the object, the measured coincidences outside (which are termed the “tails” due to their appearance in the projection data) after subtracting the randoms are all contributed from the scatter events. Thus, the scaling process is generally done by fitting the tails of the projection of the scatter estimated from the radioactivity inside the FOV to the tails of the projection data of the measured coincidences after subtracting the randoms (i.e., prompts-randoms or true+scatter events). Note that the measured coincidences after subtracting the randoms also contain the contribution due to scatter originating from radioactivity outside the FOV. The concept behind the tail-fitting process is illustrated in Fig. 1.

The lines-of-response (LORs) or sinogram bin locations of the scatter tail (i.e., regions close to the boundary of the object used to perform the tail-fitting) are defined from the transmission scan. In terms of the attenuation correction sinogram values, the bins or LORs which do not go through any object contain values of 1’s. LORs or bins corresponding to the scatter
tail region are thus defined by the attenuation sinogram values less than a threshold slightly higher than 1, where the exact threshold value is scanner dependent and reflects the accuracy of the measured attenuation map. For the HRRT a threshold value of 1.03 is used [1], [3]. The tail-fitting process is done by a least squares fit for a scatter scaling factor, $f$, minimizing

$$\sum_b (T S_b - f \cdot S_b)^2$$

(1)

where the index $b$ goes through all individual sinogram bins within the tail defined from the attenuation sinogram, $T S$ (true+scatter) is the measured coincidences after subtracting the randoms, and $S$ is the scatter estimate for the given LOR. A single scatter scaling factor is then obtained for each scatter sinogram or plane since the scatter originating from outside the FOV contributes differently for different axial planes.

The true+scatter coincidences in (1) are obtained by subtracting the measured random events from the measured prompts, either using the measured delayed coincidences window technique or the variance reduced (smoothed) randoms estimate, with the latter producing a less noisy estimate of the true+scatter coincidences. Therefore, when the random fraction (RF, defined as the ratio between the randoms and events and the prompts; i.e., randoms/prompt $\times 100\%$) is high and/or the number of acquired counts is low, the estimate of true+scatter coincidences may result in negative numbers. This may be especially true for high-resolution scanners which have hundreds of millions of LORs thus having fewer counts per LOR. Such conditions would result in negative values for the scaling factors and ultimately negative, thus unphysical scatter estimates. Typically, in order to prevent such negative and zero scaling in the scatter, a positivity-constraint is applied to the scaling factor $f$ in (1). However, the positivity-constraint is prone to introducing an overestimation bias (similar to the effect of the sinogram nonnegativity constraint described in [4], [5]) into the scatter estimate as it increases the overall mean of the scaling factors across the planes. This, in turn, leads to an underestimated activity concentration in the emission image. Another approach that prevents the negative scaling is to only use the bins with nonzero prompts and scatter within the tail region so that the prompts/randoms are almost always positive and the scaling factors are finite when performing the fit. However, this approach can also introduce an overestimation bias since the bins that correspond to nonzero prompts and scatter do not necessarily correspond to nonzero randoms in low count situations. As a result, the prompts-randoms used in the scaling process can still be overestimated.

Dynamic scanning with short-lived radioisotopes such as the $^{15}$O and $^{11}$C is particularly susceptible to such overestimation bias in the early frames [6] which tend to be short and acquired at high count rates. In particular, due to the very short half-life of $^{15}$O, a large amount of radioactivity is injected initially thus introducing a high RF. In order to capture the initial tracer distribution change as a function of time (typically corresponding to the tracer uptake stage), the framing duration is typically devised to be short. The short framing scheme leads to fewer counts within each frame thus making the scatter scaling inaccurate and likely to be biased due to the positivity-constraint at a high RF. Other examples of studies which are sensitive to the bias in the scatter estimate are those that strive to obtain image derived input functions for dynamic brain studies where the desired frame duration is between 5 to 10 s [7]. Image derived input function methods are currently of increasing interest due to an increasing number of small animal imaging studies where a sufficient number of blood samples is difficult to obtain.

We also note that in typical dynamic imaging, scattered events are generally estimated on a frame-by-frame basis. The justification for this approach is that the tracer distribution changes as a function of time, and, therefore, the scatter distribution changes accordingly. However, given the often highly variable number of events per frame typical of dynamic scanning and variable count rates at which the acquisition is performed, the number of counts in each frame might not always be sufficient to produce an accurate scatter scaling across the planes. A possible solution to this problem might be to perform the tail-fitting using the entire data set (i.e., all the bins in the tail region of the true+scatter coincidences) and obtain a single scaling factor for the scatter estimate as opposed to having different scatter scaling factors for each axial plane. However, this approach ignores the axial dependence of scatter on the activity from outside FOV and assumes that the initial estimated axial scatter distribution (i.e., without axial scaling) is accurate (which is quite uncertain especially during the early stage of the scan where there can be more activity from outside FOV). In this work, we investigate and demonstrate the bias in the conventional scatter scaling using the SSS technique for frames with high RFs and low number of counts (relevant to typical dynamic human and nonhuman primate-monkey studies) using a phantom study acquired with the high resolution research tomograph (HRRT). Furthermore, we present a robust and modular approach to scatter correction scaling: a scatter calibration technique which compensates the previously described bias and can be applied to any scatter sinograms.

II. A SCATTER CALIBRATION TECHNIQUE

The basic idea of this calibration is to have a reference scatter estimated from a frame with a relatively low RF and with a relatively high number of counts so that the estimated scatter is bias-free. For example, in dynamic studies the scatter estimated from a summed frame (with longer duration or data summed over multiple dynamic frames) can be used as the reference. This reference scatter estimate is then used to calibrate the scatter in each dynamic frame within or for some cases outside the reference frame. More specifically, a more accurate SF value (defined as the ratio between the scatter events and the sum of the true+scatter events; i.e., scatter/(prompts - randoms) $\times 100\%$) is assigned into each segment of the scatter sinograms (where segment refers to the collection of sinograms with the same oblique angle) through the calibration. Such value will be denoted as segment SF. The operation which assigns the segment SF from the reference frame into the target frame is shown

$$S_{cal}^{S_{cal}=S_{ref}(\text{Seg})} = \left( \frac{c_{sr}}{c_{tan}} \right)^{\text{Seg}} \left( \frac{c_{sr}}{c_{cal}} \right)^{\text{Seg}} S_t^{S_{ref}=S_{cal}(\text{Seg})}$$

(2)

where $S_{cal}$ is the calibrated scatter estimate (i.e., scatter sinograms for a given segment), $S_t$ is the potentially biased scatter estimate from the target frame, $c_{sr}$ is the number of scatter counts in the reference frame, $c_{cal}$ is the number of scatter...
counts in the target frame (both $c_{\text{SSS}}$ and $c_{\text{cal}}$ are obtained from the SSS estimates), $c_{\text{cal}}$ is the number of measured true+scatter counts (i.e., prompts-randoms) in the target frame, $c_{\text{est}}$ is the number of measured true+scatter counts in the reference frame, and the $S_{\text{SSS}}$ represents the segment level in which the counts are summed and their ratios are evaluated or LORs are within. Note that the calibration factors $(c_{\text{cal}}/c_{\text{SSS}})(c_{\text{cal}}/c_{\text{cal}})$ can be interpreted as the ratio of the scatter fractions between the reference and the target frames.

The assumption used in (2) is that the segment SF does not vary greatly between the target and reference frames. This implies the relative constancy of the segment SF as a function of time. This was observed to be generally the case for all studies investigated as illustrated in Fig. 2 which shows an example of the temporal behavior of the segment SF for a dynamic monkey brain study. In this case, all the frames contained enough counts to ensure that no bias was present in the scatter estimate.

An additional complication in assigning the SF values is the fact that at high count rates the measured SF may increase due to pulse pile-up; such increase is count rate (and, thus, frame) dependent. This can be explained by the fact that when pulse pile-up occurs at high count rates, it is more likely that the sum of the energies of the scattered photons gets accepted by the energy discrimination window, while the sum of the energies of the unscattered photons is more likely to get rejected by the high energy window threshold. The net result is an increase in the global SF value due to the pulse pile-up since more scatter events are accepted and more true events are rejected by the energy discrimination window. Since the RF or the count rate is typically chosen to be lower in the reference frame as compared to the target frames to minimize the bias due to high RF during the high count rate period, the SF assigned to the target frame is expected to be lower due to less pulse pile-up in the reference frame. To account for the different pulse pile-up effect for frames at different count rate, an additional correction term needs to be added to the calibration formula as shown

$$S_{f,\text{fcal}}(G) = \left(\frac{c_{\text{cal}}}{c_{\text{est}}}\right)^{(G)} S_{\text{cal}}^{\text{LORs}(G)},$$

where $S_{f,\text{fcal}}$ is the final calibrated scatter estimate, $c_{\text{cal}}$ is the number of total scatter counts from the scatter estimate obtained from performing the tail-fitting to the true+scatter coincidences without the positivity-constraint for the target frame, $c_{\text{est}}$ is the number of total scatter counts from the original calibrated scatter estimate $S_{\text{fcal}}$, and the $(G)$ represents the global level. Although the scatter estimate without the positivity-constraint is likely to contain negative scatter values, the global SF and $c_{\text{cal}}$ are unbiased and include the pulse pile-up information as will be demonstrated later. The additional correction term thus globally compensates for the change in SF due to pulse pile-up.

Equations (2) and (3) will be referred to as the segment-level scatter calibration (SSC) method from here on. The assumption used in the SSC method now becomes:

- The “pattern” in the segment SF (see Fig. 5 for a pattern example) or the relative difference in SF between the sinogram segments is consistent between the reference and the target frame.

This assumption is less constraining than the one used for only (2) since a constant temporal SF is not required, and there is no dependence on the tracer or the corresponding spatial scatter distribution. Additionally, although one can always set a pre-determined limit for the estimated global SF such as $<100\%$ when performing the scatter tail-fitting to the true+scatter coincidences, the SSC method determines a more accurate object-dependent SF value. In summary, the SSC method obtains the “pattern” in the segment SF (object shape dependent) from the reference frame and assigns an unbiased and more accurate SF value into each segment of the target scatter sinograms.

### III. METHODS

**Tomograph:** Data were acquired on the second generation of the HRRT [8], [9]. This HRRT scanner has an octagonal design, with detector heads consisting of a double 10 mm layer of LSO/LSO for a total of 119 808 detector crystals which corresponds to 4.5 billion possible LORs with no axial compression or 470 million LORs in span 3 (i.e., the LORs are axially compressed in a 1-to-1 and 2-to-1 pattern with a maximum ring difference of 67 and depth of interaction (DOI) rebinning thus giving $\sim$470 M LORs) with the sinogram dimension of $256 \times 288 \times 6367$ and the data set size of 1.8 Gb per frame for the scatter and random events and 0.9 Gb per frame for the prompts (which includes the true, scatter, and random events).

The experiments performed in this work are categorized by: (i) phantom; (ii) monkey; and (iii) human studies. By using phantom studies where the truth is known and the tracer activity distribution does not change over time, the overestimation bias in the scatter estimate and the increase in the SF due to pulse pile-up were identified. Phantom studies were also used to demonstrate the improvements achieved by the scatter calibration method. On the other hand, the monkey studies typically contain enough counts in each frame to obtain a bias-free scatter estimate while giving an environment where the tracer activity distribution changes over time thus providing a good reference to check the validity of the assumption made in the calibration method. Once the problems were identified and the assumption was validated, the calibration method was applied to the human studies, and the results were correlated to the phantom studies.
**Phantom Study:** A 20 cm long, 20 cm diameter cylindrical phantom was filled uniformly with an initial $^{11}$C radioactivity concentration of 60.9 kBq/ml. Data were grouped into sets of frames with similar numbers of counts for various RFs. The scatter estimates (using SSS) were computed for these frames in order to evaluate the accuracy of the SF for the (conventional) tail-fitting method with and without the implemented positivity-constraint in current release of Siemens software and to study the increase in the SF values at high count rates (RFs) due to the pulse pile-up effect. The framing scheme was as follows: 3 frames with $\sim 2$ M prompts, 3 frames with $\sim 5$ M prompts, 3 frames with $\sim 10$ M prompts, 3 frames with $\sim 20$ M prompts, and 1 frame with $\sim 50$ M prompts for RFs of 20%, 40%, 60%, and 75% (i.e., 13 frames for each RF). An additional frame with $\sim 2$ M prompts and 90% RF was also examined (no other number of prompts corresponded to a 90% RF in this study). These sets of numbers of counts and RFs were chosen since they are fairly representative of the number of counts encountered in human and monkey neuro-receptor imaging. The multiple frames with similar number of counts and RF were used to check the reproducibility of the SF values, and no frame data are overlapped with one another except for those with $\sim 50$ M counts which were the sum of the 2 M, 5 M, and 10 M counts frames. The count rate for these frames was at least 500 times higher than the intrinsic LSO true coincidence rate (intrinsic LSO true coincidence rate is about 100 cps) as an effort to exclude the contribution of the intrinsic LSO background to the SF value. In order to minimize the difference in scatter due to pulse pile-up, the scatter estimated from a frame with 75% RF and 300 M prompts was used as the gold standard when comparing the frames with 75% RF with and without the positivity-constraint in the scatter tail-fitting process. The gold standards for the other RFs were also obtained with at least 300 M prompts and with similar RFs except for the frame with 90% RF. The following comparisons were performed:

**(P.1) Scatter fraction (SF) comparisons:** The global SF for each aforementioned frame was calculated and plotted as a function of RF for the different numbers of acquired counts. The SF value for each segment was calculated for the frames with 90% and 75% RFs and 2 M counts with and without the positivity-constraint as well as for the gold-standard (i.e., 75% RF with 300 M counts). The segment SF was then plotted as a function of segment number, or degree of plane obliqueness (the degree of plane obliqueness increases with the absolute value of the segment number).

**(P.2) Axial uniformity comparison:** Since the SSC method assigns a more accurate and consistent SF value into each segment of the scatter sinograms, the axial uniformity of the phantom images is also expected to be improved. A frame with a more commonly observed RF of 40% and 3 M counts was used in this comparison. The fully corrected emission image for this frame was reconstructed with the conventional and SSC scatter estimates using 3D Ordinary Poisson Ordered Subset Expectation Maximization (3D-OP-OSEM) algorithm [10]. The axial uniformity of the phantom images was examined by using the axial profile with a ROI covering the whole cross section of the phantom. The emission image of the reference frame with a 40% RF and 400 M counts was also reconstructed, and its axial profile was used as the gold-standard.

**Monkey Study:** A Rhesus monkey underwent a 60 min $^{11}$C-dihydrotetrabenazine (DTBZ—a vesicular monoamine transporter VMAT2 marker) scan on the HRRT (after a 6 min transmission scan and a 5 mCi bolus injection). Data were acquired in list-mode and then framed into a $5 \times 1$ min, $5 \times 5$ min, and $4 \times 7.5$ min framing sequence. The number of counts/frame in this study ranged from 140 to 13 M with the RF ranging from 10% to 40%, and the count rate ranged between 600 and 50 kcps. The minimum number of counts per frame in this study was higher than the typical minimum number of counts in human studies; in addition, the size of the monkey’s head is smaller than that of humans so there are more prompts per plane, and the scatter estimate is less susceptible to the bias in the scatter scaling. Consequently, the conventional method was able to produce the scatter estimate free from the bias caused by low number of counts and high RF. The conventional method was thus used as the gold-standard when evaluating the performance of the calibration methods.

The early and later stages of the scan (typically corresponding to the tracer uptake and washout stage respectively) can be identified using the dead time and decay corrected true+scatter coincidence rate versus time plot. The true+scatter coincidence rate plot has been empirically observed to be a good guideline for identifying the stages of the scans/tracer phases for the studies used in this work. Here we consider the reference frame formation at two different count rates: (i) the 4 frames with similar true+scatter coincidence rate adjacent to the first frame in the early stage were grouped to form the reference frame for the calibration as shown in Fig. 3. The first frame during the early stage in dynamic brain studies typically contains a low number of counts and a high RF; thus, including this frame in the reference only increases the overall RF. As a result, although it is not the case for the monkey study used here, the first frame during the early stage of the scan was not included in the reference in order to simulate the typical condition. (ii) The entire
later stage of the scan was grouped to form the second reference frame which contains a lower count rate and RF. The SSC method was applied to the first frame in the early stage (target) using the two different reference frames as depicted in Fig. 3. The emission image of the target frame was reconstructed using 3D-OP-OSEM with the SSC and with the gold-standard scatter estimates. The difference in the emission image was investigated by dividing the SSC reconstructed image by the gold-standard one. This comparison was used to demonstrate the flexibility of the reference frame formation. It was also used to show that the SSC method does not introduce any significant bias in the reconstructed image when there are enough counts in the frame to avoid the bias in the scatter estimate under realistic experimental conditions.

**Human Study:** In order to exclude the effect of patient motion without performing any motion compensation, a human study with minimal amount of motion (～1–2 mm) was selected for the following validations. A human subject underwent a 60 min $^{11}$C-raclopride (RAC—a D2 receptor marker) scan on the HRRT (after a 6 min transmission scan and a 10 mCi Harvard pump injection). Data were acquired in list-mode and then framed into a 4 x 1 min, 3 x 2 min, 8 x 5 min, and 1 x 10 min framing sequence. The number of counts/frame in this study ranged from 57 to 2.6 M with the RF ranging from 10% to 94%, and the count rate ranged between 370 and 25 kcps. The following comparisons were performed:

**(H.1) Scatter sinogram comparisons:** The first frame of this study which contains a 94% RF and 2.6 M counts was used to examine the effect of the SSC method. The direct plane scatter sinograms and the axial scatter profiles which were placed at the centre of the radial axis in the z-r view of the scatter sinograms (see Fig. 7) for the conventional method with and without the positivity-constraint were compared with those obtained by the SSC method. For this comparison, an additional case, in which the conventional method was performed using the measured true+scatter coincidences obtained from subtracting the variance reduced randoms from the prompts instead of the raw delayed coincidences in the scatter tail-fitting process, was examined. The bias in the scatter estimate and the noisy axial scatter distribution are expected to be reduced when the variance reduced random estimate is used.

**(H.2) Segment SF comparison:** The segment SF as a function of the number of true+scatter (prompts-randoms) counts per plane was plotted for a frame with 90% RF and 2 M prompts obtained from the previous phantom study as well as for the frame obtained from the human study as described in the above comparison (H.1). The segment SF values were also compared between all the scatter estimates described in comparison (H.1).

**(H.3) Emission image comparison:** The fully corrected emission images were reconstructed with the conventional and the SSC methods using 3D-OP-OSEM. The visual comparison between the two methods is shown for one of the frames which suffered from the biased scatter scaling (i.e. tail-fitting).

**(H.4) Time activity curve (TAC) comparison for frames with short durations:** The improvement with the SSC method on frames with a very short duration is also investigated with the above human study. The first two minutes of the scan were divided into 12 x 10 s framing sequence. The number of prompts ranges from 10 k to 4 M, and the RF ranges from 95 to 50% for these short frames. The emission images were reconstructed with the conventional and the SSC methods as well as without any scatter correction using 3D-OP-OSEM. The TAC comparison was performed between these three sets of images. The accuracy of the TAC was indirectly assessed from the bias observed in the scaling factors across the axial planes due to the positivity-constraint as well as looking at the global SF without the constraint.

IV. RESULTS AND DISCUSSIONS

**Phantom Study—Comparison (P.1):** The over-scaling bias caused by the positivity-constraint in the conventional scatter tail-scaling is demonstrated in Fig. 4(a). The global SF values are reproducible with the maximum variation to be less than 5% in SF within the 3 scatter estimates obtained from similar RF and number of counts for all the frames in this study (data not shown). One can also observe the overlap of the SF values for all frames obtained without the positivity-constraint independent of the number of counts within the frame. These SF values...
also agree with the estimates obtained from a large number of counts with the constraint. The increase in the SF at high RF without the constraint is due to the pulse pile-up effect, and the information about the pulse-pile up is embedded in the tail of the measured true+scatter coincidences (as well as everywhere else) at high count rate thus producing a higher magnitude in the scatter estimate through the tail-fitting process. Note that the increase in SF when the positivity-constraint is applied contains two effects: (i) the overestimation bias due to the constraint and (ii) the pulse pile-up effect. As expected, the SF value obtained with the positivity-constraint gets closer and closer to the SF value without the constraint as the number of counts increases and as the RF decreases.

The worst case here shows a biased global SF as high as 270% obtained from a frame with 90% RF and 2 M counts. As a result, the true emission images are globally underestimated due to the oversubtraction of the scatter (see Fig. 11 for a human example). The average error in the emission image (activity concentration) is thus depicted by the difference in the SF values between the scatter estimated with and without the positivity-constraint as shown in Fig. 4(b); e.g., for a 60% RF with 2 M prompts, the average error is ~20%. Note that the error would be higher for cold spots with high densities such as the bones (i.e., high regional SF) as compared to spots with low regional SF (e.g., air) since the scatter estimate contributes differently to the emission image according to the regional SF values. In general, frames with a RF higher than 50% and with less than 20 M prompts were found to suffer significantly from the overscaling bias.

Fig. 5(a) shows the SF obtained from each segment of sinograms with and without the positivity-constraint for the frame with 90% RF and 2 M prompts. No reference was obtained for this frame due to the lack of counts for the 90% RF. One can observe that the estimated SF is higher for the more oblique segments, which contain fewer counts (i.e., negative counts are more likely to be in the true+scatter coincidences, thus, showing significant bias due to the positivity-constraint; also see Fig. 9). The segment SF obtained without the constraint shows a more reasonable value on average (mostly under 100%); however, the negative scaling of the scatter estimate is allowed without the constraint as can be seen from the negative SF values.

Fig. 5(b) shows a similar analysis to Fig. 5(a) for a frame with 75% RF and 2 M prompts with and without the positivity-constraint. A reference was obtained from a frame with 75% RF and 300 M prompts. The bias due to the positivity-constraint in the SF values is less severe in this case; also note that the SF values obtained without the constraint oscillate around the reference SF values. As described previously in the SSC method, the object shape dependent “pattern” of segment SF from the reference frame is passed to the target frame and rescaled according to the unbiased total scatter counts to separately account for the change in SF due to the pulse pile-up effect. The results after applying the SSC method are described next.

Comparison (P.2): For the axial uniformity, the standard deviation over the mean gives a measure of the relative variation from the mean. Other than compensating for the overestimation bias, the SSC method also produces a ~10% better axial uniformity by assigning a more consistent SF value into each segment of the frame with 40% RF and 3 M counts (STD/Mean = 0.073 for the conventional method, 0.065 for the SSC method, and 0.027 for the gold-standard). Note that the difference in STD/Mean between the SSC method and the gold-standard is only due to the difference in the statistics.

Monkey Study: The first row of Fig. 6 shows the gold-standard emission image of the monkey for the first frame in the early stage of the scan. The second row depicts the ratio of the SSC image to the gold-standard; the transaxial, coronal, and sagittal views are shown from left to right, respectively.
Fig. 7. The z-r view of the direct plane scatter sinograms for the first dynamic frame of the human study: (a) using (prompts-delayed coincidences) with the positivity-constraint; (b) using (prompts-delayed coincidences) without the constraint; (c) using (prompts-smoothed randoms) with the positivity-constraint; (d) using (prompts-smoothed randoms) without the constraint; (e) calibrated with SSC; and (f) the reference used for the calibration; note that the white regions in (a) to (d) are due to the saturated color scale when the intensity (counts) is too high, and the black gaps in (b) and (d) show the negative scaling of the scatter as can be observed in Fig. 8; the same color scale was used for (a) to (e) for the comparison.

emission image reconstructed with the SSC method (using the first reference frame) to the gold-standard. The color scale displays the difference within 10% of the gold-standard. The image obtained from the SSC method agrees very well with the gold standard inside the object as shown by the ratio value of 1’s. Typically, one would observe higher differences around the relatively cold regions (i.e., regions with relatively low activity) in the emission image since they are more sensitive to the change in the scatter estimate. Nevertheless, the image obtained from the SSC method shows a very good agreement even in those relatively cold regions within the object thus demonstrating that the SSC method does not introduce any significant error in the image when the conventional scatter estimate is not biased. In addition, an almost identical result (less than 1% difference) was obtained using the SSC method with the second reference frame thus showing that the reference frame formation for the SSC method is very flexible and is independent of the count rate and the spatial tracer distribution.

Human Study—Comparisons (H.1) and (H.2): Fig. 7 shows the z-r view of the direct plane scatter sinograms (i.e., the vertical axis is along the tomograph axis, and the horizontal axis is the radial distance) for the first frame of the human study which contains a RF of 94% and 2.6 M counts. The sinograms obtained with both conventional methods (using prompts-delayed coincidences with and without the positivity-constraint) show very noisy axial scatter distribution across the planes. As expected, the prompts-variance reduced (smoothed) randoms approach shows lower bias and less noisy axial scatter distribution since the tail is less noisy than that obtained from subtracting the delayed coincidences from the prompts. The sinogram calibrated with the SSC method shows a less noisy distribution across the planes with a global SF of \( \sim 47\% \).

The axial scatter profile is shown in Fig. 8. The overestimation bias can be easily observed for the conventional methods with the positivity-constraint as the estimated global SF is \( \sim 380\% \) for the prompts-delayed coincidences approach and \( \sim 280\% \) for the prompts-smoothed randoms approach; clearly there are very few counts left in the emission image after subtracting too much scatter, which agrees with our findings from the phantom study (results not shown). Also note that SF higher than 100% is physically impossible. In addition, even though the global SF for the conventional methods without the constraint are \( \sim 47\% \) which is much more accurate than the one with the constraint, the negative, highly variable, and noisier axial scatter distribution still makes it suboptimal.

The segment SF as a function of the number of \( \text{true}+\text{scatter} \) counts per plane also shows good agreement (of the scaling bias) between the phantom and human study with similar RF and number of prompts as shown in Fig. 9. There are fewer counts per plane for the more oblique segments (data not shown), and therefore the more oblique segments are more influenced by the positivity-constraint.

The segment SF comparison between all the scatter estimates described in Fig. 8 is depicted in Fig. 10. The two methods which apply the positivity-constraint show the biased pattern in the segment SF, whereas the segment SF values obtained

Fig. 8. The profiles across the planes for Fig. 7(a), (b), (c), (d), and (e) together with the corresponding global scatter fraction (SF).
Fig. 9. Comparison of segment SF versus true+scatter counts per plane within each segment using the conventional scatter estimate between the phantom and human study.

Fig. 10. The segment SF comparison between all the scatter estimates described in Fig. 8.

Fig. 11. An example of a human study which demonstrates the effect of the biased scatter on the emission image (top 3), and the same image after applying the calibration (bottom 3). The transaxial, coronal, and sagittal views are shown from left to right respectively, and the frame contains 10 M prompts with 86% RF. Note that the “hot metal-white” color scale in which the low activity regions appear to be white was chosen for better visibility of the differences.

from the two methods without the positivity-constraint oscillate around the SSC calibrated segment SF values.

Comparison (H.3): Fig. 11 shows the reconstructed emission image for a frame which suffers severely from the biased scatter estimate (with a corresponding estimated global SF of 99%) obtained from the conventional method with the positivity-constraint (top 3 images). One can observe the “apparently cold regions” as indicated by the arrows due to the biased scatter when comparing to the same image after the calibration (bottom 3 images). This example also demonstrates that even if the global SF is limited to be under 100% in the conventional scatter tail-fitting process, a significant bias can still be observed in the reconstructed image.

Comparison (H.4): A representative TAC with a ROI covering most of the activity distribution in the middle planes of the subject is shown in Fig. 12. As expected, the overestimation bias in the conventional scatter estimate occurs in all the frames; in particular, there is nothing much left in the emission image for the first 70 s. As a result, the TAC obtained from the conventional method is very inaccurate according to the bias observed in the axial scaling factors and based on the comparison of global SF with and without the constraint for each frame (data not shown). After assigning a more accurate SF value into each segment through the SSC method, a more accurate ROI value which leads to a more quantitative determination of the activity concentration can be obtained. Consequently, a significant improvement in the TAC is achieved using the SSC method in this case. Note that the TAC shown here represents the early part of the scan where the RF is high and the number of counts is low, and it is very important to the image derived input function definitions. The later part of the scan typically shows good agreement between the conventional and the proposed method as the RF decreases.

V. CONCLUSION

We have developed a scatter calibration technique which compensates for the overestimation bias and reduces the noisy axial distribution in the scatter estimates. These influences in turn improve the quantitative accuracy and axial uniformity of the reconstructed images when the number of acquired counts is low and/or with a high RF for dynamic brain imaging in high resolution PET. The scatter calibration thus provides a possible solution to the overestimation bias described in [5], and it allows one to have more freedom on making framing and scanning protocols when the bias in the scatter at low number of counts is a major concern. Furthermore, the scatter calibration method is expected to be particularly beneficial for low count $^{15}$O studies and for the image derived input functions for dynamic brain studies where one is interested in having short frames with only 5 to 10 s image duration. This calibration
can also be combined with the practical scatter approximation technique [11] to further improve the accuracy for frames with larger change in the tracer distribution during the early stage of the scan (these frames typically contain a high RF and low number of counts). In addition, the proposed method is robust and modular; it can be easily applied to any scatter sinograms and is independent of PET scanner.

REFERENCES