Impact of time-of-flight PET on quantification errors in MRI-based attenuation correction

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Short title: Impact of TOF-PET on quantification errors
ABSTRACT

Time-of-flight (TOF) PET/MRI is an emerging imaging technology with great capabilities offered by TOF to improve image quality and lesion detectability. We assess, for the first time, the impact of TOF image reconstruction on PET quantification errors induced by MRI-based attenuation correction (MRAC) using simulation and clinical PET/CT studies.

METHODS: Standard 4-class attenuation maps were derived by segmentation of CT images of 27 patients undergoing PET/CT examinations into background air, lung, soft tissue and fat tissue classes, followed by the assignment of predefined attenuation coefficients to each class. For each patient, 4 PET images were reconstructed: non-TOF and TOF both corrected for attenuation using reference CT-based attenuation correction (CTAC) and the resulting 4-class MRAC maps. The relative errors between non-TOF and TOF MRAC reconstructions were compared with their reference CTAC reconstructions. The bias was locally and globally evaluated using volumes of interest (VOIs) defined on lesions and normal tissues and CT-derived tissue classes containing all voxels in a given tissue, respectively. The impact of TOF on reducing the errors induced by metal-susceptibility and respiratory-phase mismatch artifacts was also evaluated using clinical and simulation studies.

RESULTS: Our results show that TOF-PET can remarkably reduce attenuation correction artifacts and quantification errors in the lungs and bone tissues. Using class-wise analysis, it was found that the non-TOF MRAC method results in an error of $-3.4 \pm 11.5\%$ in the lungs and $-21.8 \pm 2.9\%$ in bones, whereas its TOF counterpart reduced the errors to $-2.9 \pm 7.1\%$ and $-15.3 \pm 2.3\%$, respectively. The VOI-based analysis revealed that the non-TOF and TOF methods resulted in an average overestimation of 7.5% and 3.9% in/near lung lesions ($n = 23$) and underestimation of <5% for soft tissue and in/near bone lesions ($n = 91$). Simulation results showed that as TOF resolution improves, artifacts and quantification errors are substantially reduced.

CONCLUSION: TOF-PET substantially reduces artifacts and improves significantly the quantitative accuracy of standard MRAC methods. Therefore, MRI-based attenuation correction should be less of a concern on future TOF PET/MR scanners with improved timing resolution.
Key Words: TOF, PET/MRI, attenuation correction, quantification, whole-body imaging.
INTRODUCTION

Hybrid PET/MR imaging has recently emerged as a new modality enabling simultaneous molecular and morphological assessment of a variety of physiopathological conditions (1). Over the last two decades, PET/MR technology has experienced considerable technical advances toward addressing the challenges encountered in system design and quantitative performance. With the advent of avalanche photodiodes and silicon photomultipliers (SiPMs), the challenge of mutual compatibility between PET and MR subsystems has now been well addressed, thus paving the way toward fully integrated time-of-flight (TOF) PET/MR systems (2). However, accurate PET quantification using MRI-based attenuation correction (MRAC) remains a major challenge (3).

MR signals are related to proton density, relaxation time properties of tissues and the selected pulse parameters. Therefore, there is no a unique mapping between MR intensities and attenuation coefficients at 511 keV, as in PET/CT. Moreover, bones cannot be well delineated on conventional MR sequences because of their low water content and short transverse relaxation time. Truncation of MRI field-of-view (FOV) and metal-induced susceptibility artifacts are other problems encountered in MRAC (4). Generally, MRAC methods can be categorized in 3 groups: segmentation-based approaches, which segment MR images into different tissue classes (background air, lung, fat, and soft tissue) and assign predefined attenuation coefficients to each class (5), atlas registration based approaches, in which a co-registered MR-CT atlas dataset is used to derive a pseudo CT image from the patient’s MR image (6) and emission-based approaches in which the attenuation map is directly estimated from TOF-PET emission data with MR anatomical prior information (7,8). Currently, segmentation-based MRAC is the standard approach on commercial PET/MR scanners.

In 3- or 4-class MRAC methods, bones are replaced by soft tissue and the inter/intra-patient heterogeneity of attenuation coefficients in different tissue classes is ignored, which leads to quantification errors in the estimation of standardized uptake value (SUV) ranging between 4 and 25% in different organs (9-13). Using PET/CT datasets of 35 patients, Martinez-Möller et al. reported an average SUV error of 8.0 ± 3.3% in 21 bone lesions and <5% in all other lesions (5). Schulz et al. reported, using 15
whole-body PET-CT/MR patient scans, an average error of 6.5 ± 4.1% in 7 bone lesions and a maximum error of −13.4% in a pelvic bone lesion (14). Ouyang et al demonstrated that if the bones can be identified in MR images to produce a 5-class MRAC map, SUV errors in all bones are reduced to <10% (10). Ultra-short echo time (UTE) pulse sequences have been extensively explored to include bones as 5th class and reduce PET quantification errors (15). Despite the promising results, UTE sequences are time-consuming and not yet clinically feasible.

With the advent of clinical TOF-PET systems, several studies reported that TOF can improve PET image quality in terms of signal-to-noise ratio, lesion detectability, convergence rate and tolerance to inconsistencies between emission and correction data compared to non-TOF reconstructions (16). Using 2D phantom simulations, Boellaard et al. showed that TOF-PET reconstruction can reduce PET quantification errors when using MR-based attenuation correction (17). In fact, in TOF-PET, the difference in arrival times of coincident annihilation photons are measured with an uncertainty governed by the timing resolution of the detectors. During PET image reconstruction, the additional TOF information is exploited to update image voxels only along segment of responses, defined by TOF resolution, instead of the whole line of response. Consequently, the cross-dependencies between image voxels are reduced, which results in reduced noise propagation, fast and space-invariant convergence, thus improving the detectability of lesions located near large hot regions (e.g. the liver), and reduced sensitivity to errors in normalization, attenuation and scatter corrections.

Considering the fast development of TOF-PET detectors toward sub-100 ps coincidence timing resolutions (18) and the lack of clinical studies highlighting the importance of TOF in MRAC PET, we aim at systematically evaluating the impact of TOF on PET quantification errors induced by 4-class MRAC. In addition, we evaluate the performance of TOF-PET in the presence of metal susceptibility and respiratory mismatch artifacts in MRAC maps. To explore the trend of bias reduction in future generation PET/MR scanners with improved timing resolution, we conduct realistic 3D simulations using different TOF resolutions in phantoms derived from clinical FDG examinations.
MATERIALS AND METHODS

Data Acquisition and Image Reconstruction

PET/CT datasets were acquired on the Siemens Biograph mCT Flow scanner (Siemens Healthcare, Erlangen). The PET subsystem of the scanner consists of 4 rings of 48 detector blocks, covering axial and transaxial FOVs of 218 and 700 mm, respectively. PET data were acquired with an effective TOF resolution of 580 ps and reconstructed using an ordinary Poisson ordered subset expectation maximization (OSEM) algorithm with point spread function (PSF) and TOF. The default manufacturer-provided reconstruction parameters for OSEM+PSF with and without TOF were 2 iterations and 21 subsets, and 2 iterations and 24 subsets, respectively. The whole-body image matrix size was 200×200 with 4×4×2 mm³ voxels. The CT subsystem is a 128-slice CT scanner (SOMATOM Definition AS+) with an extended transaxial FOV of 780 mm.

Clinical Studies

A total number of 27 patients (13 women, 14 men; average age 58.8 ± 18.2 years) referred for ¹⁸F-FDG (n = 25) and ¹⁸F-Choline (n = 2) PET/CT examinations were included in this study. The institutional ethics committee approved this retrospective study. The patients had an average body mass index (BMI) of 25.1 ± 4.2 kg/m². They were injected by a standard dose of ¹⁸F-FDG (250.5 ± 44.4 MBq) and ¹⁸F-Choline (329.1 ± 1.2 MBq). After an uptake time of 60 and 10 minutes for FDG and FCH administrations, whole-body PET/CT FlowMotion™ scanning was performed for two scan ranges, from the toes to the mid thigh with bed speed of 1.1 mm/sec. and from the mid thigh to the vertex with speed of 0.7 mm/sec. The average acquisition time was 24.9 ± 5.4 minutes. A whole-body CT scan protocol was performed for PET attenuation correction using 100-120 kVp, 150 mAs, and 5 mm slice thickness.

Simulation Studies
To explore the limiting impact of TOF on MRAC PET quantification errors, we conducted a series of 3D analytic simulations with different TOF timing resolutions using an in-house TOF-PET simulator, developed for the native geometry of the Siemens mCT system using MATLAB with SPMD parallel processing. The software was validated using the experimental NEMA phantom. Effective timing resolutions of 580, 350 and 100 ps were modeled to respectively represent typical TOF resolution of first generation of clinical TOF-PET/MR scanners, introduced since 2010 (19), current generation of SiPM-based TOF-PET scanners (2) and future generation PET scanners with the best possible timing resolution currently achievable in the laboratory (18). Realistic whole-body phantoms were derived from clinical FDG PET/CT studies to simulate the biodistribution of FDG, patient-specific CTAC map, the respiratory-phase mismatch between PET and MRAC images. TOF sinogram data and actual attenuation factors were obtained by forward projection of activity and attenuation maps. Poisson noise realizations were simulated for 80 M counts. The contribution of scattered and random coincidences was ignored. The PET activity maps were reconstructed for 4 overlapping beds with a matrix size of 200×200×109 per bed, using an ordinary Poisson OSEM algorithm with 3 iterations and 28 subsets for non-TOF, and 3 iterations and 21 subsets for TOF reconstructions.

**Attenuation Map Generation**

To derive MRAC maps, CT images of patients were segmented into 4 tissue classes: background air, lung, fat, and non-fat soft tissues. Background air and lungs were segmented using a seeded region growing technique implemented in the ITK-SNAP software (20). The fat tissue class was segmented by thresholding CT intensity values between –470 and –53 Hounsfield units (corresponding to attenuation coefficients at 511 keV between 0.05 and 0.095 cm⁻¹). The soft tissue class was then defined as the complement of the segmented classes. In this procedure, bones and air pockets are assigned to soft tissue class. Mean attenuation coefficients of 0, 0.0221, 0.0864 and 0.0975 cm⁻¹ were assigned to background air, lungs, fat and non-fat soft tissue classes, respectively. Owing to intrinsic differences in image contrast
between CT and MR imaging, the resulting 4-class attenuation maps might differ from the scanner’s 4-
class MRAC maps in tissue content. Supplemental Figure 1 compares both attenuation maps of a patient
who underwent a PET/MRI scan on the Philips Ingenuity PET/MR scanner (19) and a complementary
PET/CT scan where an excellent coregistration was achieved. As can be seen, both attenuation maps are
in good agreement with sparse differences in fat content.

**Data Analysis**

Four PET image reconstructions were performed for each patient: reference CTAC-PET and MRAC-PET
with and without TOF. The relative quantification error (bias) in tracer uptake was calculated on a voxel-
by-voxel basis (i) for each patient as follows:

\[
\text{Bias}_{i}^{m} = 100 \times \frac{(SUV_{\text{MRAC}})_{i} - (SUV_{\text{CTAC}})_{i}}{(SUV_{\text{CTAC}})_{i}}
\]

where \( m \) is the reconstruction method (non-TOF or TOF). The difference in bias of the non-TOF and TOF
methods was then evaluated using volume of interest (VOI) and class-wise analyses. For each patient, 13
VOIs were defined on normal tissues including the lungs (upper, middle and lower portions of left and
right lungs), liver, aorta, cerebrum, 3rd thoracic (T3), 4th lumbar (L4) and illia of pelvis (left and right).
Moreover, 80% isocontour VOIs were defined on the lesion locations in TOF CTAC-PET images. Lesions
were classified into 3 groups: soft tissue \( (n = 44) \), bones and/or near bone \( (n = 47) \) and lungs and/or near
lung \( (n = 23) \). For class-wise analyses, the original CT images were down-sampled to the resolution of
PET images and segmented using region-growing and thresholding techniques into lungs, fat, soft tissue
and bones. The distributions of some VOIs and tissue classes for a representative patient are shown in
Supplemental Figure 2. For the defined VOIs, the mean (\( \mu \)), standard deviation (\( \sigma \)) and root-mean-squared
error (RMSE) of bias \( (\sqrt{\mu^2 + \sigma^2}) \) was calculated. The correlation between MRAC-PET and CTAC-PET
with and without TOF was determined on scatter plots using Pearson correlation analysis. The
concordance between the SUVs was evaluated using Bland-Altman plots. The limits of agreement were
calculated from logarithmically transformed values. The statistical significance of differences in SUV bias was also evaluated using the Wilcoxon signed-rank test. The differences were considered statistically significant for \( P \)-values < 0.05.

RESULTS

Clinical Studies

Figure 1 shows the bias maps of PET images reconstructed using non-TOF and TOF MRAC for two patients with different BMIs. The maps show that the maximum errors occur over the bones, lungs and air gaps. They are substantially reduced by TOF-PET reconstruction. Table 1 summarizes the mean, standard deviation (SD) and RMSE of SUV_{mean} bias between non-TOF MRAC-PET and CTAC-PET, and TOF MRAC-PET and CTAC-PET images in different VOIs located in normal regions and lesions, and defined tissue classes.

Figure 2A compares the mean and SD of SUV_{mean} bias between non-TOF and TOF PET images in VOIs defined on different tissues with normal tracer uptake. In this figure, the marker points show the mean of bias in each VOI, whereas the horizontal bars and vertical boxes indicate the mean and 2 SDs of bias between VOIs in each region. For the VOIs defined on the lungs \((n = 162)\), the non-TOF MRAC resulted in an underestimation of \(-1.0 \pm 16.6\%\) with a RMES of 16.7\%, while its TOF counterpart yielded an error of \(-1.5 \pm 8.0\%\) with a RMSE of 8.1\% (Table 1). For the total VOIs defined on T3/L4 vertebra, pelvis and cerebrum \((n = 135)\), non-TOF and TOF methods resulted in an average bias error of \(-16.7 \pm 5.6\%\) with a RMES of 17.6\% and \(-9.8 \pm 4.8\%\) with a RMES of 10.9\%, respectively. Similarly, for all VOIs defined on soft tissues, aorta and liver \((n = 54)\), non-TOF and TOF methods showed an average bias of \(-3.9 \pm 5.2\%\) with 6.5\% RMSE and \(-3.4 \pm 3.5\%\) with 5.3\% RMSE, respectively. The statistical analysis of the results revealed that the difference in the bias performance of non-TOF and TOF MRAC methods is significant over the vertebra, pelvis and cerebrum \((P < 0.001)\), while there is no proof of statistically significant differences in the lungs \((P = 0.587)\), aorta \((P = 0.961)\) and liver \((P = 0.067)\).
Figure 2B shows the mean ± SD of bias between non-TOF and TOF-PET images in VOIs defined on lesions, grouped into 3 categories depending on their location: soft tissue, for lesions seated in fat and non-fat tissues ($n = 44$), (near) bone, for lesions located on bones or on soft tissues close to bone ($n = 47$) and (near) lungs, for lesions located in the lungs or in the immediate vicinity of the lungs, mainly the mediastinal lymph nodes ($n = 23$). The results presented in Table 1 show that in soft tissue and (near) bone lesions the non-TOF and TOF MRAC methods result in underestimation of SUV$_{\text{mean}}$ with comparable RMSE biases of 5.3 vs. 4.1% and 8.8 vs. 7.0%, respectively. For lesions located in/near lungs, the methods overestimate the SUV$_{\text{mean}}$. TOF MRAC method, however, showed an improved performance by achieving a bias of 3.9 ± 9.2% (10.0% RMSE) compared to its non-TOF counterpart with a bias of 7.5 ± 14.6% (16.4% RMSE). The statistical analysis showed that there is a significant difference in bias performance of the methods in soft tissue ($P = 0.023$) and in/near lungs ($P = 0.019$) lesions, while there is no proof of statistically significant differences in/near bone lesions ($P = 0.624$).

Figure 2C compares the mean ± SD of bias between non-TOF and TOF methods in non-fat soft tissue, fat, lung and bone tissue classes. Each marker point represents the mean of bias in each patient, calculated over all voxels belonging to the tissue classes. According to the results summarized in Table 1, the RMSE bias performance of the two methods is <5% in all voxels in soft and fat tissue classes. In fat tissue class, both methods overestimate the SUV. However, the TOF MRAC method was found to reduce both the mean and SD of the bias. Over the bones, an underestimation of −21.8 ± 2.9% (21.9% RMSE) and −15.3 ± 2.3% (15.5% RMSE) was achieved by non-TOF and TOF methods, respectively. Similarly, the methods showed underestimations of −3.4 ±11.5 (11.9% RMSE) and −2.9 ± 7.1% (7.7% RMSE) in the lungs, respectively. TOF PET reconstruction resulted in a significant difference in all tissue classes ($P < 0.001$) except the lungs ($P = 0.613$).

The MRAC PET images were further analyzed for SUV correlation and concordance with respect to CTAC PET images. Figure 3 (top panel) shows the scatter plots of SUV$_{\text{mean}}$ in all normal tissues and lesions in PET images reconstructed using MRAC and CTAC with and without TOF, with correlation coefficients and corresponding regression equations. Overall, there is a good correlation between non-
TOF MRAC and non-TOF CTAC SUV values with $R^2 = 0.980$, which is improved by TOF reconstruction ($R^2 = 0.993$). Figure 3 (bottom panel) shows the Bland-Altman concordance analysis of the MRAC methods. Differences and limits of agreement (LA) are expressed as a function of the average SUVs of PET/MR and PET/CT. The regression lines of the difference (indicated with percent slope) show a systematic underestimation of SUV for both non-TOF and TOF MRAC methods (−8.1% and −7.5%, respectively). The results show that the TOF reconstruction can reduce the bias and the SD of bias.

Figure 4 compares the non-TOF and TOF PET images of a patient presenting with metal-induced susceptibility artifacts in MRAC maps. The patient had a PET/MRI and a complementary PET/CT scan. The MR and CT images were non-rigidly registered. The void regions induced by the metal implant were then transferred to the derived 4-class CTAC map. As can be seen, the TOF reconstruction can substantially reduce the artifacts close to the hip implant. Figure 5 compares PET images of a patient with respiratory-phase mismatch between PET and MRAC maps. As pointed by the arrows, one of the lesions is indiscernible in non-TOF PET image due to the under-correction caused by respiratory-phase mismatch artifacts. However, the TOF reconstruction has effectively suppressed the artifacts, thus improving lesion detectability.

**Simulation studies**

Figure 6 shows the PET, actual CTAC and MRAC images used in our non-TOF and TOF simulations, together with the bias maps corresponding to non-TOF and TOF images with timing resolutions of 580, 350 and 100 ps. Note that for each simulated TOF resolution, two PET images were reconstructed (using reference CTAC and 4-class MRAC maps). The results clearly show that PET quantification errors induced by the 4-class maps are reduced as the timing resolution is improved, especially over the bones. Class-wise analyses showed that over bones, the non-TOF reconstruction results in an underestimation of $-25.15 \pm 9.8$ (27.0% RMSE), which is reduced to $-19.3 \pm 6.66$ (20.42% RMSE), $-16.63 \pm 5.4$ (17.51% RMSE) and $-12.47 \pm 3.23$ (12.88% RMSE) using TOF reconstructions with timing resolutions of 580,
350 and 100 ps, respectively. For the non-TOF and TOF with 580, 350, 100 ps resolutions, RMSEs of bias averaged over all tissue classes except bones, were 13.11%, 9.15%, 8.61% and 8.28%, respectively. The impact of TOF reconstruction on respiratory-phase mismatch artifacts was further evaluated in a simulated clinical FDG scan (Figure 7). A respiratory-phase mismatch was simulated between the actual CTAC and MRAC maps with 12-mm displacement of diaphragm as if the MRI was acquired at the end of inspiration. A 4-mm spherical tumor was also inserted in the PET image to simulate a case where respiratory-phase mismatch impaired the detectability of a liver lesion. As shown in the figure, the activity of the tumor and superior border of liver were suppressed due to white-band banana artifacts. As the timing resolution improves, the tumor and liver lobe become more discernible and lean toward their actual uptake. The bias maps also demonstrate that improved TOF resolution reduces quantification errors.

DISCUSSION

To the best of our knowledge, this is the first clinical study highlighting the impact and importance of time-of-flight in MRAC PET image reconstruction. Using VOI-based and class-wise analyses, we demonstrated that TOF can reliably compensate for erroneous MRAC maps especially over the bone and lungs where the maximum errors occur. The results of 135 VOIs defined in/near bone regions with normal tracer uptake showed an average underestimation of 16.7% and 9.8% for non-TOF and TOF MRAC reconstructions, respectively. Class-wise evaluations showed that these methods result in maximum underestimation of 21.8% and 15.3% over the bones, respectively. Our non-TOF results are consistent with the >15% errors reported in (9) using PET/MR datasets. The VOI-based evaluation of 47 in/near bone lesions showed an average 5% error for both methods, which is in agreement with the 8% and 6% errors reported in (5,14). Consistent with observations made in (5,11), the results of 164 VOIs in normal tissues of the lungs showed an average SUV underestimation <2% for non-TOF and TOF methods. However, non-TOF MRAC showed a large standard deviation (16.6%), which was substantially reduced by TOF (8.1%). The reason for this large SD is that the standard MRAC methods do not take the
intra/inter-patient variability of lung attenuation coefficients into account and assign a constant value for the lungs in all patients. Our results showed that non-TOF MRAC results in 7.5% overestimation of in/near lung lesions, which is reduced to 3.9% by TOF image reconstruction. For soft tissue lesions, the results showed that both methods give rise to <5% errors, which is in agreement with previous studies (5,14).

Our study also demonstrated a strong correlation between PET/MR and PET/CT SUVs in normal tissues and lesions. It was found that using TOF PET image reconstruction, the dispersion of data points around the regression line is reduced, especially for lesions, resulting in a higher coefficient of determination. The Bland-Altman plots revealed a limited concordance between PET/MR and PET/CT measurements in particular for lesions with high SUVs. As a result, both non-TOF and TOF methods showed a systematic bias, proportional to average SUVs. Nonetheless, the limit-of-agreement results showed that TOF can reduce the standard deviation of errors.

In this study, we used the default vendor-provided reconstruction parameters of 2/24 and 2/21 iterations/subsets for the non-TOF and TOF reconstructions, respectively. Indeed, the non-TOF reconstruction do not result in the same convergence rate achieved by TOF reconstruction. Achieving the same convergence rate for lesions using both reconstruction methods is hardly accomplished in clinical setting, since it depends on the size and location of the lesions and lesion-to-background ratio, which varies for different lesions and patients. However, we evaluated SUV quantification errors of non-TOF and TOF MRAC methods using different iterations for one clinical study. As shown in Supplemental Figure 3, the bias changes with iteration number, especially in bones with non-TOF reconstruction. The results show that the bias introduced by TOF MRAC is almost steady for all tissue classes except bones. Consequently, the TOF MRAC method resulted in significantly less bias compared to its non-TOF counterpart for each iteration. Our simulation results demonstrated that as TOF timing resolution improves toward 100 ps, targeted for future TOF-PET/MR scanners, SUV quantification errors induced by inaccurate MRAC maps are substantially reduced, thereby improving the level of accuracy of PET quantification.
CONCLUSION

In this work, we evaluated the impact of TOF PET image reconstruction on SUV quantification errors caused by standard MR segmentation-based attenuation correction of PET data using simulation and clinical studies. Our results demonstrated that TOF capability can substantially reduce the mean and standard deviation of bias over the lungs and bones. It was found that non-TOF MRAC results in 11.9% and 21.9% root-mean-squared errors in the lungs and bones, respectively. These errors are reduced to 7.7% and 15.5%, respectively, when using TOF. The results showed that the root-mean-square errors of non-TOF and TOF methods in soft tissue and fat regions are less than 5%. From a clinical perspective, our study suggests that as the timing resolution of TOF-PET/MR scanners improves, PET quantitative accuracy for bone and lung lesions increases.

DISCLOSURE

The authors declare no conflict of interest.

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Figure 1. Representative bias maps between PET images corrected for attenuation using 4-class MRAC and CTAC techniques obtained using non-TOF and TOF reconstructions for two patients with large (left panel) and low (right panel) BMIs.
Figure 2. Relative errors of mean SUV estimations between MRAC-PET and reference CTAC-PET images reconstructed with and without TOF in (A) normal tissues, (B) lesions and (C) various tissue classes. Means and 2 standard deviations are indicated by horizontal bars and vertical boxes, respectively.
Figure 3. Top panel: Scatter plots showing results of linear regression analysis between SUV\textsubscript{mean} in different VOIs of MRAC-PET and reference CTAC-PET with and without TOF. Bottom panel: Bland-Altman plots of SUV\textsubscript{mean} for MRAC-PET and reference CTAC-PET with and without TOF. Differences and limits of agreement (LA) are expressed as a function of average SUVs of PET/MR and PET/CT.
**Figure 4.** Comparison of non-TOF and TOF PET images in the presence of metal-induced susceptibility artifacts on MRAC attenuation map.
Figure 5. Comparison of non-TOF and TOF PET images in the presence of respiratory-phase mismatch between MRAC attenuation map and corresponding PET images.
Figure 6. Simulation of the impact of TOF reconstruction on PET quantification errors of MRAC method. Top panel: The PET activity, CTAC and 4-class MRAC maps derived from a whole-body FDG-PET scan. Bottom panel: The bias maps between MRAC-PET and CTAC-PET images for different timing resolutions.
Figure 7. Simulation of the impact of TOF reconstruction on the reduction of artifacts induced by respiratory-phase mismatch between PET and MRAC images. Top: PET activity, CTAC and 4-class MRAC maps derived from a whole-body FDG-PET scan. Middle: the PET image reconstructed using different TOF timing resolutions. Bottom: the corresponding bias maps between MRAC-PET and CTAC-PET images.
TABLE 1. PET quantification bias [Mean ± SD, (RMSE)] of non TOF vs. TOF in different VOIs and tissue classes.

<table>
<thead>
<tr>
<th>VOI</th>
<th>non TOF</th>
<th>TOF</th>
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<tbody>
<tr>
<td>Lung</td>
<td>–1.0 ± 16.6% (16.7%)</td>
<td>–1.5 ± 8.0% (8.1%)</td>
</tr>
<tr>
<td>T3/L4</td>
<td>–16.8 ± 5.8% (17.7%)</td>
<td>–8.8 ± 4.9% (10.1%)</td>
</tr>
<tr>
<td>Pelvis</td>
<td>–18.7 ± 5.2% (19.4%)</td>
<td>–10.8 ± 5.0% (11.9%)</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>–12.5 ± 3.3% (13.0%)</td>
<td>–9.7 ± 4.1% (10.5%)</td>
</tr>
<tr>
<td>Aorta</td>
<td>–2.8 ± 6.7% (7.3%)</td>
<td>–3.2 ± 3.9% (5.1%)</td>
</tr>
<tr>
<td>Liver</td>
<td>–5.2 ± 2.8% (5.8%)</td>
<td>–4.7 ± 2.9% (5.5%)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>–1.8 ± 4.9% (5.3%)</td>
<td>–2.5 ± 3.2% (4.1%)</td>
</tr>
<tr>
<td>(Near) Bone</td>
<td>–5.2 ± 7.2% (8.8%)</td>
<td>–4.6 ± 5.2% (7.0%)</td>
</tr>
<tr>
<td>(Near) Lung</td>
<td>7.5 ± 14.6% (16.4%)</td>
<td>3.9 ± 9.2% (10.0%)</td>
</tr>
<tr>
<td>Soft</td>
<td>–1.5 ± 1.8% (2.4%)</td>
<td>–2.0 ± 1.7% (2.6%)</td>
</tr>
<tr>
<td>Fat</td>
<td>2.4 ± 3.0% (3.8%)</td>
<td>0.5 ± 1.7% (1.7%)</td>
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<tr>
<td>Bone</td>
<td>–21.8 ± 2.9% (21.9%)</td>
<td>–15.3 ± 2.3% (15.5%)</td>
</tr>
<tr>
<td>Lung</td>
<td>–3.4 ± 11.5 (11.9%)</td>
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