

# Supplementary Material:

## Plane-dependent ML Scatter Scaling: 3D Extension of the 2D Simulated Single Scatter (SSS) Estimate

**Abstract.** When the ML-scaled scatter estimates are used, an improved agreement is obtained between MLEM reconstructions using CT-based attenuation correction and MLAA reconstructions, where the attenuation and activity images are jointly estimated, indicating that the ML-scaled scatter estimate is more accurate than the SSS and the FT-SSS estimates.

### 1. Activity Reconstruction

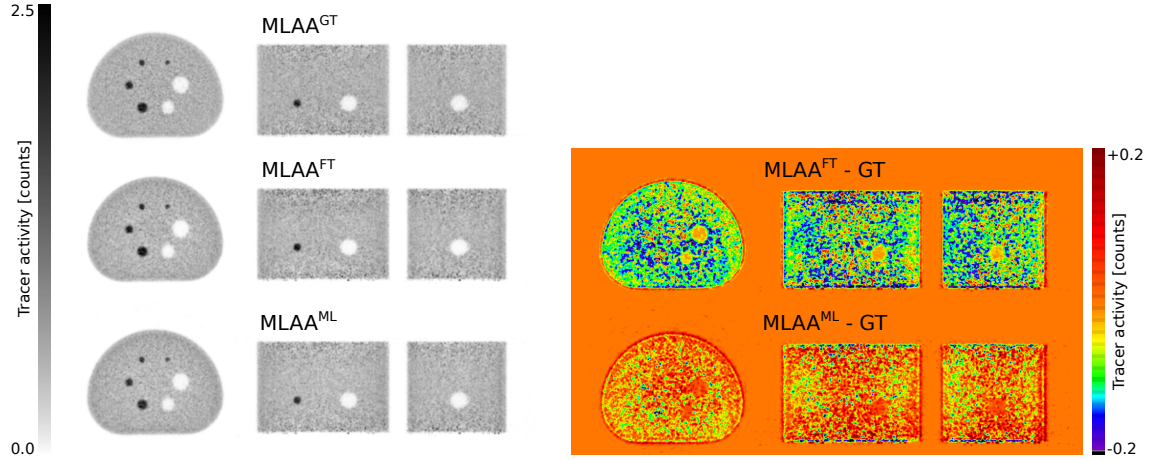
Maximum likelihood activity and attenuation (MLAA) reconstructions were obtained using the CT-derived SSS, FT-SSS and the ML-SSS estimates for scatter correction. MLAA produces an attenuation map and an activity image. In the analysis, this activity image is not used. Instead, “standard” reconstructions are computed, by computing MLEM reconstructions with 3 iterations and 24 subsets using the attenuation map produced by MLAA. This allows us to compare MLAA and MLEM activity images all obtained with the same iteration scheme but with different scatter estimates (namely SSS, FT-SSS and ML-SSS). In the following, we will refer to these images as the (“standard”) MLAA activity reconstructions. Recall that the MLAA algorithm estimates the activity only up to a multiplicative scale factor. In order to eliminate any confounding effects of this scale factor in the reconstructions, the scale problem in MLAA was fixed by imposing the total tracer activity of the reference MLEM reconstruction.

### 2. Monte-Carlo Simulation Study

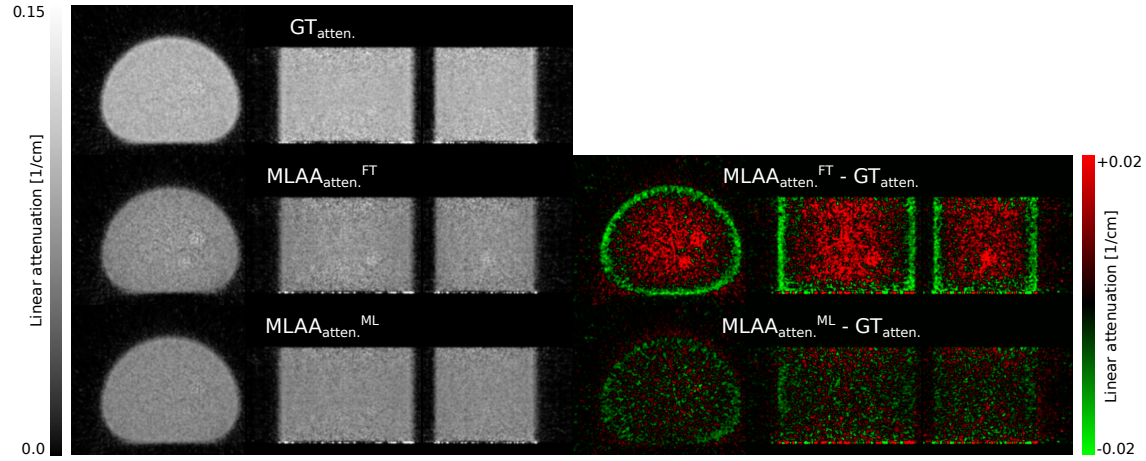
Figure S.1a shows the MLAA activity reconstructions as well as their difference compared to the ground truth MLEM activity reconstruction when the FT-SSS and the ML-SSS estimates were used for scatter correction of the TOF-PET emission data.

A different bias structure is observed when comparing the MLAA difference images of figure S.1 to the difference images of figure 3 with the FT-SSS and the ML-SSS estimates. Although the MLEM activity reconstruction with the ML-SSS estimate has produced a slightly different noise profile compared to the ground truth, it seems to be free of any systematic bias. A similar behaviour is also observed for the activity reconstructions of MLAA. Interestingly however, a different bias structure is observed when comparing the MLEM and MLAA activity reconstructions when the FT-SSS used for scatter correction. We computed the absolute voxel-by-voxel difference of MLAA and

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(a) MLAA activity reconstructions (left) and their difference images (right) compared to the ground truth MLEM activity reconstruction obtained by reconstructing the true prompts. The difference images were obtained by using the FT-SSS (center) and the ML-SSS (bottom) estimates for scatter correction. The top left MLAA activity reconstruction was obtained by reconstructing the true prompts only.



(b) MLAA attenuation reconstructions (left) and their difference images (right) compared to the ground truth MLAA attenuation reconstruction (top left) (obtained by reconstructing the true prompts) when the FT-SSS (center) and the ML-SSS (bottom) estimates were used for scatter correction.

Figure S.1: MLAA activity (a) and attenuation (b) reconstructions of the Monte-Carlo TOF-PET emission data.

MLEM reconstructions compared and normalized to the ground truth MLEM activity reconstruction. The results are summarized in table S.1.

Moreover, it is interesting to see that the MLAA activity reconstructions seem to be more robust to the inconsistencies in the FT-SSS estimate values than MLEM activity reconstructions. This is best seen in the difference images near plane 14, indicated with an arrow in figure 3. Close to this plane, the FT-SSS scatter estimate was more overestimated than in the neighbouring planes, as revealed by the dip of the GT scale in figure 2a. This overestimation causes a locally increased bias in the activity image, but

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Table S.1: Absolute voxel-by-voxel difference of MLAA and MLEM reconstructions when the FT-SSS and the ML-SSS estimates are used for scatter correction compared to the ground truth (GT) activity reconstruction.

	MLEM - GT	MLAA - GT	MLAA - MLEM
FT-SSS	17.8%	18.3%	8.1%
ML-SSS	3.8%	7.3%	5.9%

this bias is less pronounced in the  $\text{MLAA}^{\text{FT}}$  image than in the  $\text{MLEM}^{\text{FT}}$  image. Since MLEM and MLAA have different degrees of freedom (i.e. while MLEM estimates a total of  $J$  unknowns, which is the total number of image voxels, MLAA estimates  $2J$  unknowns from the same TOF measurement) during reconstruction, it could be expected that they respond differently to possible inconsistencies in the shape and magnitude of the scatter estimate.

Figure S.1b shows MLAA attenuation reconstructions when the FT-SSS and the ML-SSS estimates are used for scatter correction as well as the difference images of these reconstructions compared to the ground truth attenuation ( $\text{GT}_{\text{atten.}}$ ) reconstruction (obtained by applying MLAA to the unscattered simulated emission data). The simulation demonstrates that when the data are corrected with an inaccurate scatter estimate signs of “cross-talk” (imprints of the hot spheres in the activity reconstruction) appear in the attenuation reconstruction. However, when the more accurate ML-SSS estimate is used for scatter correction the previously observed “cross-talk” artifacts are markedly reduced from the reconstructions.

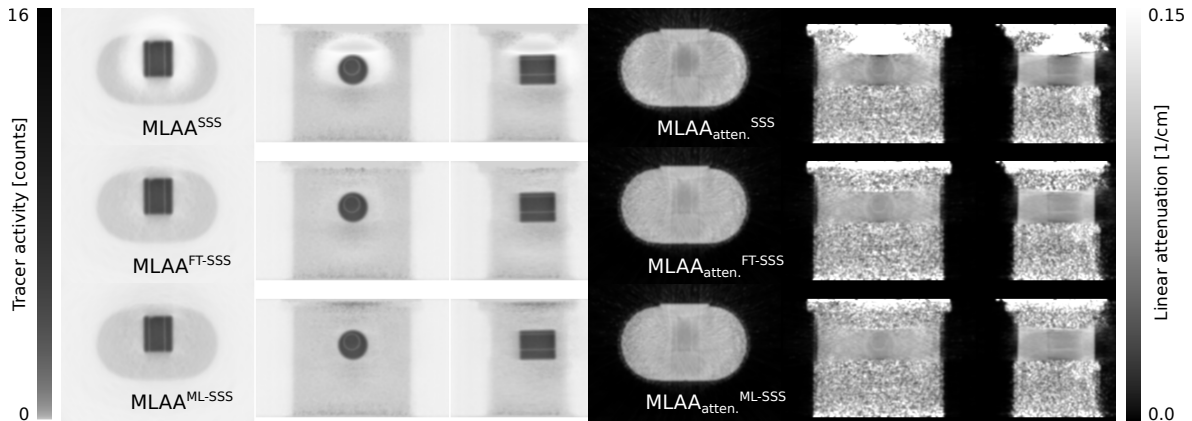


Figure S.2: MLAA activity (left) and attenuation (right) reconstructions when the SSS (top), FT-SSS (center) and the ML-SSS (bottom) estimates were used for scatter correction.

### **3. Phantom Data**

Figure S.2 shows MLAA activity and attenuation reconstructions of the phantom measurements. When the SSS estimate is used for scatter correction, parts of the data inconsistency are manifested in the attenuation reconstruction. However, when the ML-SSS estimate is used, the activity and attenuation reconstructions seem to be affected by artefacts the least. The absolute voxel-by-voxel difference of MLAA reconstructions compared and normalized to MLEM activity reconstructions (avoiding the first/last 9 planes at the axial extents of the phantom support) using the SSS, FT-SSS and ML-SSS estimates were 21.1%, 17.2% and 16.6%, respectively.

### **4. Patient Data**

In addition to MLEM activity reconstructions, “standard” MLAA activity reconstructions were obtained of all our patient datasets correcting for scatter using the SSS, the FT-SSS as well as the ML-SSS estimates. We computed the differences between MLEM and MLAA activity reconstructions in a region near the bladder. Near the bladder, patient motion during the PET-scan and between the PET-scan and the CT-scan is expected to be very small in most patients, and in such a case, MLEM and MLAA are expected to agree well. Figure S.3 shows the relative difference of the tracer activity in the bladder region of interest (ROI) of the MLAA activity reconstruction compared and normalized to the MLEM activity reconstruction of the same ROI for all the patients in our dataset. Overall, MLEM and MLAA reconstructions seemed to agree the most when the ML-SSS estimate was used for scatter correction, which as before seems to agree with the Monte-Carlo simulation experiment. On average, the relative difference between MLEM and MLAA reconstructions in the bladder region using the SSS, FT-SSS and ML-SSS estimates for scatter correction was 13.8% ( $\pm 8.2\%$ ), 16.0% ( $\pm 8.5\%$ ) and 9.2% ( $\pm 7.0\%$ ), respectively.

### **5. Discussion**

This work is by no means an attempt to fully validate the simultaneous activity and attenuation reconstructions of MLAA. A comprehensive quantitative analysis of MLAA activity reconstructions compared to the clinical gold-standard (MLEM with CT-based attenuation correction) is beyond the scope of this study and results on the validation of the method can be found in (Boellaard et al. 2014). Instead, we used the difference between MLAA and MLEM activity reconstructions as an indicator of data consistency. Since the MLAA and MLEM methods estimate a different number of parameters from the TOF-PET emission data, the two algorithms may respond differently to any possible inconsistencies in the data. Interestingly, we observed that in case of an inaccurate scatter estimate (i.e. SSS or FT-SSS estimates) the MLAA activity reconstruction provided a slightly more accurate result compared to the MLEM activity reconstruction.

## REFERENCES

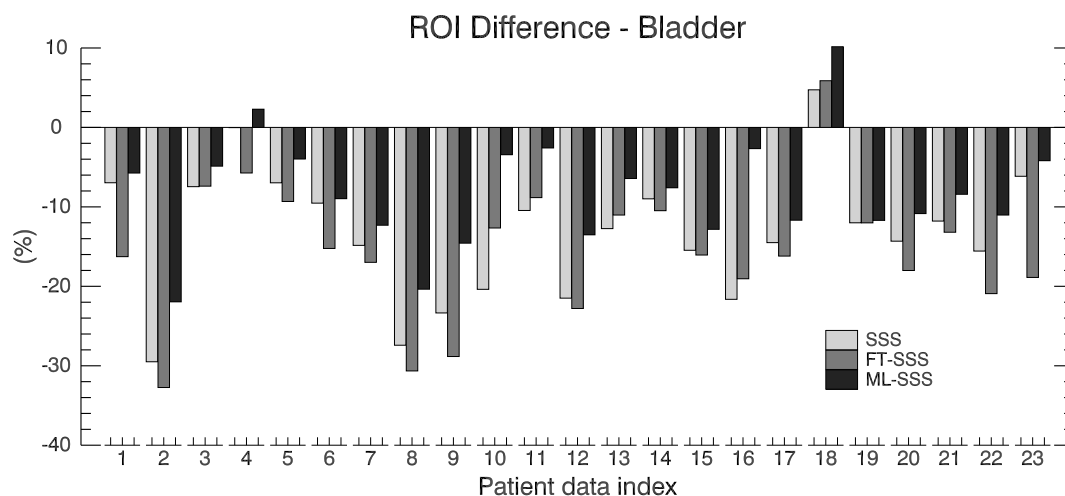


Figure S.3: Relative difference of “standard” MLAA and MLEM activity reconstructions in the bladder ROI for all the patients in our dataset.

However, visual inspection suggested that parts of the inconsistent scatter estimate were now absorbed in the MLAA attenuation reconstruction. Furthermore, in some patients the agreement between MLEM and MLAA improved dramatically for the bladder region.

## References

Boellaard, R., M. B. M. Hofman, O. S. Hoekstra, and A. A. Lammertsma (2014). “Accurate PET/MR Quantification Using Time of Flight MLAA Image Reconstruction”. In: *Mol. Imaging Biol.* 16.4, pp. 469–477.