Lesion contrast recovery for partial-volume averaging: Quantitative correction or qualitative enhancement?

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Partial-volume averaging refers to the blurring effects that occur in diagnostic imaging of adjacent tissues with different anatomical or physiological properties such as density (with x-ray CT) or tracer activity (with PET). In the context of PET imaging for the detection of atherosclerotic lesions, accurate quantification of tracer activity in lesions that are smaller than approximately the scanner resolution $\times 2$ can pose a significant challenge. The reconstructed image resolution of current-generation PET scanners is in the range of 4-8 mm full-width-at-half-maximum (FWHM), depending on the particular algorithms employed, e.g., using standard ordered subsets expectation maximization (OSEM-STD) or point-spread-function modeling for added resolution recovery (OSEM-PSF). Therefore, for small lesions below 10-15 mm diameter, there is significant under-estimation of lesion activity and lesion-to-background (LBR) contrast.

In the recent article by Cal-Gonzalez *et al*,[1] the authors used an image post-processing technique called the local projection (LP) method to improve lesion quantification accuracy, and subsequently proposed to reconstruct 'partial-volume-corrected' (PVC) images. In Figure 1, their reported data are used to plot the simulated lesion contrast values before and after LP-estimation and PVC-reconstruction. The LP method is based on a critical assumption that the exact spatial location and extent of the lesion can be identified and then used to 'focus' the measured PET activity into the a-priori-defined lesion volume.

Two lesion segmentation methods were proposed to identify the 'a-priori' lesion volume for LP-enhancement, but both have potential limitations that should be clarified. The first method used x-ray CT imaging of coronary calcium (Ca) to define the lesion volume needed to help 'focus' the NaF PET activity using the described algorithms. The sequential acquisition of the CT and PET studies can lead to difficulties in registration due to inter-scan patient motion. Indeed six of the 17 cases in this study required manual co-registration which is reliant on the ability to accurately visualize the site of enhanced NaF uptake on the CT scan. In addition, while the spatial resolution of CT (0.5-1.0 mm) is clearly able to improve lesion size estimation vs PET, the assumption that NaF activity is uniformly co-localized within the calcified plaque may not be reliable. The lesion activity values obtained using the proposed PVC-CT method should be interpreted with caution, since NaF is a tracer of active calcification, and is known to not necessarily co-localize with the extent of total (stable or inactive) calcification.[2,3] Obtaining a quantitatively accurate NaF signal concentration requires that the activity focused into the lesion be associated with the correct volume of calcium. The authors noted in their discussion that ''no significant correlations were observed between 18F-NaF plaque uptake in the uncorrected images and CT-based calcifications. However, in the new PVC-reconstructed images, a significant correlation of 18F-NaF uptake and calcification density of the atherosclerotic plaque was observed…'' Locally concentrating or 'focusing' the NaF activity within a smaller or denser CT volume will, by design, lead to an increase in the (inverse) correlation. Observation of the improved correlation supports that the algorithm is

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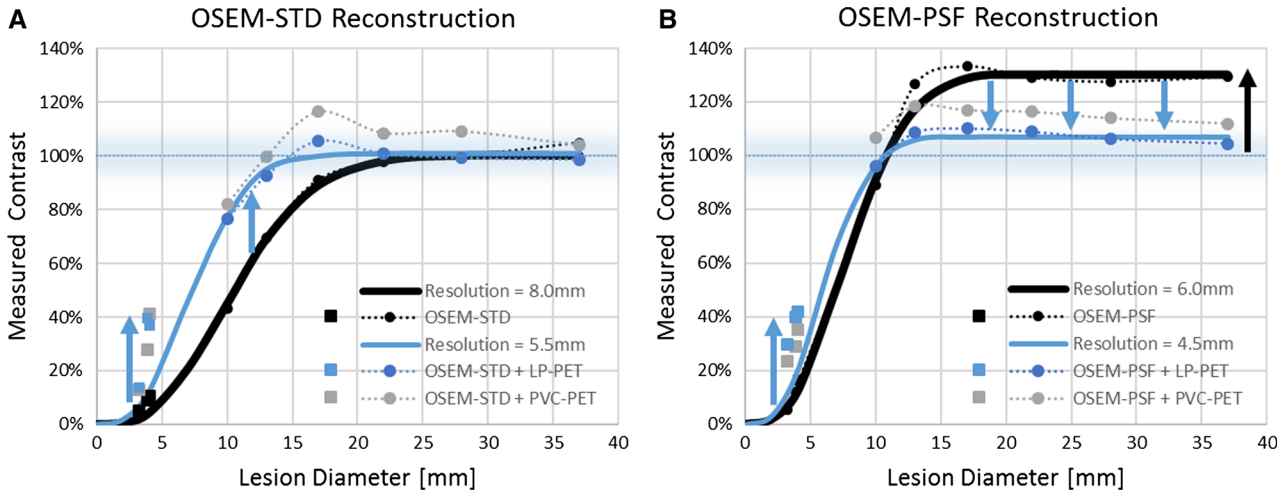

Figure 1. Measured lesion to background (LBR) values using (**A**) standard (OSEM-STD) and (**B**) resolution recovery (OSEM-PSF) image reconstruction, before (*black*) and after LP-estimation (*blue*) and PVC-reconstruction (*gray*). *Circles* are NEMA phantom *spheres*, and *squares* are thorax phantom lesions. For the OSEM-STD images (**A**), the LP-estimation improved contrast recovery (*blue arrows*) for simulated lesions <20 mm diameter, while maintaining accuracy for the larger lesions at very close to 100% of the known true values. For the OSEM-PSF images (**B**), the LP-estimation improved contrast recovery for simulated lesions <5 mm diameter (*blue arrow left*), and also improved accuracy for the larger lesions (*blue arrows right*), which were originally over-estimated (*black arrow*) at 130% of the known true values..

behaving as expected. Indeed the phantom results show that, where the underlying assumptions are correct, the LP-estimation algorithm can provide a more accurate estimate of NaF activity concentration. Thus, in the case of the patient studies, the results are very promising, but the strength of the underlying assumptions is unclear and additional validation against gold-standard measurements is needed to support the assertion that the observed correlation was ''due to the better quantitative evaluation of 18F-NaF uptake in the calcified plaques.'' While the PVC-reconstructed lesions in the patient images certainly display enhanced contrast vs background activity, additional objective studies are needed to determine whether the method can be used to reliably improve quantification and lesion detection accuracy (i.e., sensitivity and specificity) in comparison to an accepted gold-standard. Studies of this nature have been performed by comparing PET-CT imaging results to histopathology assessment of excised carotid artery plaques for example.[4]

The second segmentation method used the initial reconstructed PET images themselves to estimate the lesion volume, employing a background-corrected thresholding technique. While this is not strictly independent 'a-priori' information defining the lesion volume, it does not impose the added assumption or requirement (or potential benefit) of accurate co-localization with CT-Ca as described above. Therefore, this method may be more applicable for PET imaging of small lesions in general, using highly specific tracers such as NaF. It is very interesting to observe that despite the much lower spatial resolution of PET- vs CT-based segmentation, the LP-estimated contrast values were still significantly improved vs the original images reconstructed using OSEM-STD and OSEM-PVC (Figure 1 blue vs black points). However, it is important to note that the lesion must first be visible above the background activity in the original reconstructed PET image for this method to apply. Also, for lesions much smaller than the PET image resolution, the estimated 'a-priori' size can never appear smaller than the FWHM resolution, limiting the incremental benefit of the LP method. This is likely why the LP-estimated and PVC-corrected values were still substantially under-estimated for the simulated thoracic lesions of 3-4 mm diameter.

For the OSEM-STD reconstruction of spherical lesions in a uniform background, the LP method was shown to significantly improve the measured contrast for spheres <15 mm diameter (consistent with an effective spatial resolution $\approx$5.5 mm) while maintaining quantitative accuracy for the larger spheres (Figure 1A). Contrast was also improved in smaller simulated lesions (3-4 mm diameter) in the thorax phantom, but these were not fully 'partial-volume-corrected' back to the known reference value.

While the OSEM-PSF reconstructions demonstrated higher contrast for the spherical lesions due to improved spatial resolution of 6 vs 8 mm in the OSEM-STD

images, the quantitative values were actually over-estimated by 30% due to edge-enhancement 'ringing' artifacts visible in the larger spheres >15 mm diameter, as previously reported by Nuyts *et al*[5] In this case, the LP-estimation method again improved quantitative accuracy of the simulated lesions, whereas the PVC-reconstructed images showed enhanced contrast but reduced accuracy for all lesion sizes compared to the LP method.

For both the OSEM-STD and OSEM-PSF reconstructions, the LP post-processing estimation of lesion activity appeared to be more accurate than the subsequent PVC-reconstructed images, which consistently demonstrated improved lesion contrast but were still quantitatively less accurate. LP-estimation showed more incremental benefit in effective resolution for STD vs PSF reconstruction, and resulted in more quantitatively accurate lesion contrast values for both reconstruction methods; therefore, the added value of PVC-reconstruction is unclear, beyond qualitative image enhancement.

In summary, the LP-estimation and PVC-correction results presented by Cal-Gonzalez *et al*[1] can provide significant benefits in quantitative accuracy and lesion contrast enhancement, but are highly dependent on (i) the accuracy of anatomical lesion segmentation and (ii) co-registration of lesion anatomy and physiology. Additional in vivo imaging vs ex vivo validation studies are warranted to further characterize the methods for detection and quantification of atherosclerotic lesions using NaF PET-CT.

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