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Direct Reconstruction of CT-based Attenuation Correction Images for PET with Cluster-Based Penalties

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Abstract

Extremely low-dose CT acquisitions used for PET attenuation correction have high levels of noise and potential bias artifacts due to photon starvation. This work explores the use of *a priori* knowledge for iterative image reconstruction of the CT-based attenuation map. We investigate a maximum *a posteriori* framework with cluster-based multinomial penalty for direct iterative coordinate decent (dICD) reconstruction of the PET attenuation map. The objective function for direct iterative attenuation map reconstruction used a Poisson log-likelihood data fit term and evaluated two image penalty terms of spatial and mixture distributions. The spatial regularization is based on a quadratic penalty. For the mixture penalty, we assumed that the attenuation map may consist of four material clusters: air+background, lung, soft tissue, and bone. Using simulated noisy sinogram data, dICD reconstruction was performed with different strengths of the spatial and mixture penalties. The combined spatial and mixture penalties reduced the RMSE by roughly 2 times compared to a weighted least square and filtered backprojection reconstruction of CT images. The combined spatial and mixture penalties resulted in only slightly lower RMSE compared to a spatial quadratic penalty alone. For direct PET attenuation map reconstruction from ultra-low dose CT acquisitions, the combination of spatial and mixture penalties offers regularization of both variance and bias and is a potential method to reconstruct attenuation maps with negligible patient dose. The presented results, using a best-case histogram suggest that the mixture penalty does not offer a substantive benefit over conventional quadratic regularization and diminishes enthusiasm for exploring future application of the mixture penalty.

Index Terms

PET/CT; ultra-low dose attenuation correction; penalized weighted least squares; cluster-based mixture penalty

I. Introduction

PET/CT imaging plays a critical role in diagnosis, staging and therapy planning for oncologic patient management [1–4]. In PET/CT imaging, the CT image helps with anatomical localization of PET tracer uptake and also provides attenuation correction of the PET data. In this study, we are concerned with respiratory-gated PET/CT imaging, which can improve the quantitative accuracy of the PET imaging, thus being beneficial for cancer diagnosis, radiation therapy planning, and the quantitative assessment of response to therapy [5, 6].

Here, we focused on CT-based attenuation correction, which is essential to quantitative respiratory PET imaging. Ideally, respiratory-gated PET imaging requires phase-matched respiratory-gated CT-derived attenuation maps. Respiratory motion inconsistencies between the CT and PET images can cause inaccuracies in the attenuation correction and result in artifacts at organ boundaries in PET images [7, 8]. To compensate for this mismatch, respiratory-gated CT images can be acquired over multiple time phases within one respiratory cycle to improve the estimate of respiratory motion in the CT images. However, the acquisition of multiple CT images for respiratory-gating leads to a substantially increased radiation dose to patient [9]. Since the additional radiation dose of extended duration CT-based attenuation map acquisitions is considered unacceptable in clinical practice, several suboptimal approaches were proposed using single-phase CT scan at end-expiration or averaged CT images over one respiratory cycle in cine or low-pitch helical scan modes [10–13].

To reduce the radiation dose in diagnostic CT imaging, several low dose CT scan protocols have been developed with reduced tube current, selection of appropriate tube voltage, and addition of hardware filtration for radiation dose reduction of 4D CT [14–17]. It is necessary to use noise suppression techniques to prevent the deterioration of signal-to-noise ratio and the introduction of bias and artifacts in CT images from low-dose acquisitions [18–20]. With decreasing tube current, some groups investigated the effects of denoising techniques in the sinogram [21–25] or image domains [26–28], or statistical image reconstruction techniques with more accurate noise models of the detection process [29–31] or different prior/regularization functions [32, 33]. Additional dose reduction can be achieved with sparse-view acquisition and compressed sensing recovery techniques based on dictionary learning or total variation in the CT images [34–37].

For CT-based attenuation correction in PET/CT imaging, however, it is possible to reduce radiation dose by at least a factor of 10 compared to the ‘low-dose’ diagnostic CT methods described above [16], reaching an even lower dose level which we loosely term ‘ultra-low dose CT’ (ULDCT). ULDCT scans induce a high level of noise and bias artifacts in images due to photon starvation as illustrated in Fig. 1. Although the low dose CT protocols can be applied to obtain CT-based attenuation correction images over multiple time phases, which are matched well with respiratory motion in PET images, it is essential to enhance the deteriorated signal-to-noise ratio in CT images to avoid inappropriate PET attenuation correction. To suppress image noise and bias in this noise regime we explore the use of a

novel mixture penalty function, which is based on the expected intensity histogram of a PET 511 keV attenuation map, in a maximum *a posteriori* (MAP) reconstruction framework (Section II). The two unique aspects in this study are the derivation of direct PET attenuation map reconstruction and the use of a mixture penalty. Section III evaluates the performance of the proposed direct reconstruction of the attenuation map with simulation studies. Section IV and V discuss and conclude the comparison results of different reconstruction techniques from our simulations.

II. Methods

A. Direct PET Attenuation Map Reconstruction

We investigate a maximum *a posteriori* (MAP) framework for direct iterative image reconstruction of the CT-based attenuation map at 511 keV:

$$\hat{\mu}_{511} = \underset{\mu_{511}}{\operatorname{argmin}} \{ \tilde{L}(\mu_{511}) + \beta U_Q(\mu_{511}) + \gamma U_M(\mu_{511}) \}. \quad (1)$$

In (1), the negative Poisson log-likelihood of the measurement is approximated as a weighted least square problem [38]:

$$\tilde{L}(\mu_{511}) = \frac{1}{2} \sum_i W_i (g_i - \hat{g}_i)^2, \quad (2)$$

where μ_{511} is an attenuation map of 511 keV photons, and $\mathbf{g}$ and $\hat{\mathbf{g}}$ are the measured and estimated CT sinograms in the attenuation domain as measured with the CT system. In (2), $\mathbf{W}$ is a diagonal weight matrix with elements inversely proportional to the variance of the CT data. The CT sinogram can be estimated directly from an attenuation map of 511 keV (μ_{511}) as

$$\hat{g}_i = \sum_j D_{ij} T_c(\mu_{511}; j) = \sum_i D_{ij} \mu_{CT; j}. \quad (3)$$

In (3), the direct CT forward projector is composed of two successive transformations through $T_C()$ and $\mathbf{D}$. $T_C()$ is an energy-dependent bilinear conversion operator from PET to CT attenuation maps (μ_{CT}):

$$\mu_{CT} = T_c(\mu_{511}) = \mathbf{C}_1 \mu_{511} + \mathbf{C}_2 \quad (4)$$

, where $\mathbf{C}_1$ and $\mathbf{C}_2$ are the coefficient vectors of the bilinear conversion operator. The bilinear conversion operator uses two different scaling coefficients for regions of lung and the bone [39, 40]. We incorporated the bilinear energy conversion into the forward operator to apply penalties onto 511 keV attenuation map during image reconstruction. $\mathbf{D}$ is a system

matrix to compute line integrals for a fan-beam CT system and was modeled with the distance-driven method [41].

B. Penalty Function

The penalty term in (1) is expressed by the weighted combination of two functions, the spatial (U_Q) and mixture (U_M) penalties. β and γ are strength parameters of the spatial and mixture penalties. The spatial penalty is commonly employed for this application and is a potential function of the Gibbs distribution for Markov random fields. We used quadratic (Q) form, which is a smoothing penalty based on the local intensity difference between adjacent voxels [42, 43]:

$$U_Q(\mathbf{\mu}) = \sum_j \sum_{k \neq j} \frac{n_{jk}}{2} (\mu_j - \mu_k)^2, \quad (5)$$

where μ_k is the neighbor voxel of μ_j . We chose 8 neighbors of the current j -th voxel for the Q-penalty. The mixture (M) penalty is a novel contribution of this work, and is based on the attenuation intensity histogram of $\mathbf{\mu}_{511}$:

$$U_M(\mathbf{\mu}) = - \sum_j \log\{p_M(\mu_j)\}. \quad (6)$$

The M-penalty takes advantage of the fact that most attenuation intensity histograms at 511 keV have only a few distinct peaks corresponding to specific body materials (demonstrated in Fig. 2). The M-penalty encourages each voxel, μ_j , to belong to one distinct material in the histogram. These types of penalties have been proposed in the past for similar applications [44–48]. In our application, we hypothesize that the mixture penalty can reduce artifacts due to biased threshold values in ultra-low dose data without the resolution loss that typical results from a high level of quadratic smoothing.

The M-penalty consists of mixtures of probability density functions (pdfs). The mixture pdf, $p_M()$ is defined by the weighted sum of up to four functions: an exponential and three Gaussian distributions for the 4 different material clusters of tissue: air, lung, soft tissue, and bone (indexed by $k=1, 2, 3$, and 4, respectively):

$$p_M(\mu_j) = \alpha_{1,j} f^{\text{exp}}(\mu_j | \lambda) + \sum_{k=2}^4 \alpha_{k,j} f^{\text{Gauss}}(\mu_j | m_k, \sigma_k), \quad (7)$$

where λ is the rate parameter of exponential distribution and m_k and σ_k are mean and standard deviation of Gaussian distribution. For the air-background cluster, an exponential distribution (f^{exp}) is used and for other clusters of lung, soft tissue, and bone, three different Gaussian distributions (f^{Gauss}) are employed.

$$f^{\text{exp}}(x|\lambda) = \begin{cases} \lambda e^{-\lambda x}, & x \geq 0 \\ 0, & x < 0 \end{cases} \quad (8)$$

$$f^{\text{Gauss}}(x|m, \sigma) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(x-m)^2}{2\sigma^2}\right) \quad (9)$$

The $\alpha_{k,j}$ is the mixture proportion (weight) of the k^{th} material cluster basis for the j^{th} voxel. The M-penalty will promote voxels values close to the most common attenuation coefficients of air, lung, soft tissue, and bone materials. The adjustable mixture weights allows each voxel have a unique mixture pdf based on an estimate of the materials in the voxel. If the weights were fixed, the mixture penalty would not change for different voxels and different regions of the image; this would lead to incorrect penalty values for less common regions. For example, bone regions have a relatively low weight and an objective function with fixed weights would essentially force all voxels to have values different from bone attenuation. The adjustable weights allow for more flexibility in estimating values for different regions.

C. Iterative Coordinate Decent (ICD) Optimization

To optimize the cost function for direct reconstruction of μ_{511} in (1), which has the form of a penalized weighted least square problem, we employed the iterative coordinate decent (ICD) method [49]. ICD method solves and updates successively the cost according to (10).

$$\frac{\partial E(x)}{\partial x} = \frac{\partial}{\partial x} \{ \tilde{L}(x) + \beta U_Q(x) + \gamma U_M(x) \} \Big|_{x = \hat{\mu}_{511,j}^{(n)}} = 0 \quad (10)$$

We use the Newton-Raphson algorithm partly to compute a root of the likelihood term in (10) at the n -th iteration depending on the previous estimate:

$$\frac{\partial \tilde{L}(x)}{\partial x} \Big|_{x = \hat{\mu}_{511,j}^{(n)}} = \tilde{L}'(\hat{\mu}_{511,j}^{(n-1)}) + \left\{ (\hat{\mu}_{511,j}^{(n)} - \hat{\mu}_{511,j}^{(n-1)}) \tilde{L}''(\hat{\mu}_{511,j}^{(n-1)}) \right\}. \quad (11)$$

The first and second derivatives of the approximate likelihood function are:

$$\tilde{L}'(\hat{\mu}_{511,j}^{(n-1)}) = -C_{1,j} \sum_i W_i D_{ij} (g_i - \hat{g}_i^{(n-1)}) \quad (12)$$

$$\tilde{L}''(\hat{\mu}_{511;j}^{(n-1)}) = C_{1;j}^2 \sum_i W_i D_{ij}^2. \quad (13)$$

The derivatives of Q- and M-penalty functions are:

$$\left. \frac{\partial U_Q(x)}{\partial x} \right|_{x=\hat{\mu}_{511;j}^{(n)}} = \sum_{k \neq j} n_{jk} (\hat{\mu}_{511;j}^{(n)} - \hat{\mu}_{511;k}^{(n)}) \quad (14)$$

$$\left. \frac{\partial U_M(x)}{\partial x} \right|_{x=\hat{\mu}_{511;j}^{(n)}} = - \left. \frac{p'_M(x)}{p_M(x)} \right|_{x=\hat{\mu}_{511;j}^{(n)}} \quad (15)$$

$$p'_M(x) = [-\alpha_{1,j}^{(n-1)} \lambda^2 e^{-\lambda x}] + \sum_{k=2}^4 \left[\frac{-\alpha_{k,j}^{(n-1)} (x - m_k)}{\sqrt{2\pi} \sigma_k^3} \exp\left(\frac{-(x - m_k)^2}{2\sigma_k^2}\right) \right] \quad (16)$$

The derivative of M-penalty at the n-th iteration was derived with the mixture proportions, $\alpha_{k,j}^{(n-1)}$ determined from the previous n-1 iteration to avoid a dependence on the updated estimate of μ_{511} .

Table I outlines the direct ICD (dICD) algorithm for reconstruction of the 511 keV attenuation maps. Filtered backprojection (FBP) produces an initial image for dICD reconstruction, and the mixture proportions for each voxel are initialized from the initial FBP image. During dICD optimization, a half-interval search (HIS) method finds a root of (10) as a new estimate of μ_{511} . Then, based on the new value of the j^{th} voxel, the mixture weights, $\alpha_{k,j}$ of the k -th tissue clusters in the M-penalty is updated. The function parameters λ and m_k and σ_k , $\forall k=1,2,3,4$ of the exponential and Gaussian pdfs in M-penalty are pre-determined based on intensity histograms of typical attenuation maps and do not change during reconstruction.

In this study, we limit the mixture penalty to be a combination of only two functions (selected from the four possible tissue functions) at each voxel. This is implemented by setting the mixture weights to be inversely proportional to the intensity difference between the current estimate for the j^{th} voxel and the mean (m_k) of the k^{th} cluster-pdf, where only clusters with mean values adjacent to the current estimate are used. When the new estimate is greater than m_4 (mean) of the bone cluster function, nonzero weights are assigned only to the bone cluster and to the most attenuating soft tissue cluster as described by the second row of equation (17). And, the mixture weights for the non-adjacent clusters are set to zero.

$$\begin{cases} \alpha_{k,j} = \frac{m_{k+1} - \mu_j}{m_{k+1} - m_k} \text{ and } \alpha_{k+1,j} = \frac{\mu_j - m_k}{m_{k+1} - m_k}, & m_k \leq \mu_j^{(n)} \leq m_{k+1} \\ \alpha_{3,j} = \frac{\mu_j - m_4}{2\mu_j - m_3 - m_4} \text{ and } \alpha_{k,j} = \frac{\mu_j - m_3}{2\mu_j - m_3 - m_4}, & \mu_j^{(n)} > m_4 \\ 0, & \text{otherwise} \end{cases} \quad (17)$$

These $\alpha_{k,j}$ updated with each iteration, provide a unique pdf curve for each voxel and the estimated values are promoted to be distributed similarly to their unique pdf.

D. Simulation and Evaluation

For both CT and PET analytic simulations, we used the NCAT chest phantom [50]. For polychromatic CT simulation, we used an x-ray energy spectrum (w_m) of 120 kVp, which is sampled at each 1 keV over 120 energy bins as shown in Fig. 3(A). We generated energy-dependent attenuation maps over polychromatic x-ray energy bins from a NCAT phantom. Fig. 3(B) and (C) show attenuation maps at two different x-ray energies of 0.5 and 119.5 keV. Using energy histogram and energy-dependent attenuation maps, a noise-free (NF) CT sinogram ($\mathbf{g}_{\text{NF}}(E_m) = \mathbf{D}\boldsymbol{\mu}_{\text{CT}}(E_m)$) was computed from the energy-dependent NCAT CT phantom for each energy bin, E_m , through line integral computation with a distance-driven method [41]. We then performed an exponential conversion of the noise-free sinograms followed by a multiplication of the influx x-ray intensity I_m ($I_m = I_0 w_m$) at m -th energy bin to convert it to the intensity domain. After adding Poisson quantum noise to the noise-free polychromatic intensity domain sinograms, all polychromatic sinograms were energy integrated over 120 energy bins. Gaussian electronic noise (standard deviation of σ_e) was added into the integrated polychromatic sinogram, prior to log conversion:

$$\mathbf{I}_{\text{scan}} = \left[\sum_m \text{poisson} \{ E_m I_m \times \exp(-\mathbf{g}_{\text{NF}}(E_m)) \} \right] + N(0, \sigma_e) \quad (18)$$

Due to addition of Gaussian noise and subsequent mean dark current subtraction, non-positive values can exist in $\mathbf{I}_{\text{scan}}$ especially at low CT dose level. To allow for the logarithm operation, we applied a ‘flip’ non-positivity correction in which negative values had their sign changed, and zero values were set to a nominal low positive ε . We chose a ε as a minimum positive sinogram value as described below. Finally, we take the logarithm of the non-positive corrected sinogram to get a noisy realization in the attenuation domain:

$$\mathbf{g} = \log \left(\frac{I_0}{\max[\|\mathbf{I}_{\text{scan}}\|, \varepsilon]} \right) = \log \left(\frac{\sum_m I_m}{\max[\|\mathbf{I}_{\text{scan}}\|, \varepsilon]} \right). \quad (19)$$

We generated polychromatic sinograms under two different noise levels corresponding to a low dose (LD) level and ultra-low dose (ULD) scans. ULD data was 20 times lower than LD by changing I_0 (total integrated x-ray intensity) from 40000 to 2000. For the non-positivity

correction, ε set to 0.24 and 0.0003 for LD and ULD data. We did not perform beam-hardening correction prior to image reconstruction. The sinogram bias was computed as:

$$\text{Bias} = \frac{1}{I} \sum_i [\mathbf{g}_i^{\text{noisefree}} - \mathbf{g}_i^{\text{noisy}}]. \quad (20)$$

In (20), I is the number of sinogram elements and $\mathbf{g}^{\text{noisefree}}$ is the simulated noise-free sinogram. We computed the bias for the two different noise levels.

The user-defined PET phantom has three hot 3 cm circular lesions or targets in the soft tissue and lung regions. For PET simulation, we set the activity ratio of lesion, soft tissue, and lung as 4:2:1. Attenuation ($\mathbf{p}_{\text{AC}}$) and noise-free PET ($\mathbf{p}_{\text{NF}}$) sinograms were computed through a forward projection of the PET system from a positron-emitting tracer distribution and the energy-converted 511 keV NCAT CT phantom. An approximately clinical level of Poisson noise was added into the attenuated PET sinogram (total of 1.04×10^6 events), using

$$\mathbf{p} = \text{Poisson}\{\mathbf{p}_{\text{NF}} \times \exp(\mathbf{p}_{\text{AC}})\}. \quad (21)$$

The noisy attenuated PET sinogram was corrected by CT-based attenuation maps and then were reconstructed by FBP with a Hanning filter. We used FBP for the PET data since the intent of this study was to evaluate the impact of the CT reconstruction methods on PET attenuation correction, and not the bias and variance from photon-limited PET data.

To define the M-penalty function, parameters of the normalized exponential and Gaussian pdf functions were estimated from the attenuation intensity histogram of the reference image. The reference image was reconstructed using FBP with a ramp filter from very high-dose CT data and energy-scaled to 511 keV. Table II summarizes the fitted parameters to define the normalized exponential in (8) and Gaussian pdfs in (9) from the histogram of the reference image. Fig. 4(A) shows the fitted curves (red solid line) from the reference intensity histogram (blue opened dot) and the normalized pdf curve (black solid line) with same fitted parameters. The histogram and fitted curve follow scales on the left y-axis and pdf curve on the right. The mixture proportions $\alpha_{k,j}$ of each material pdf to define a mixture pdf related to one voxel was determined based on the current estimate of j -th voxel described in (17). Fig. 4(B) shows the dependency of mixture proportions on three different voxel intensities ($\mu_1=0.001$, $\mu_2=0.005$, and $\mu_3=0.0105$) resulting in three different mixture pdfs. For example, in the case of $\mu_3=0.0105 \text{ mm}^{-1}$ in Fig. 4(B), since it located between soft tissue and bone pdfs and it is closer to the mean of the soft tissue pdf, the mixture pdf for a voxel with this value would be weighted towards a soft tissue pdf and will promote values close to the mean of the soft tissues. Through the iterative adjustment process of mixture proportions during the image reconstruction, the voxel will be encouraged to belong to one attenuation coefficient among air, lung, soft tissue, and bone materials.

The image quality was evaluated in terms of root mean squared error (RMSE) over the body region in both the CT-based attenuation coefficient maps and PET images:

$$\text{RMSE} = \sqrt{\frac{\sum_{j \in \text{Body}} (\mu_j - \hat{\mu}_j)^2}{N}}. \quad (22)$$

N is the number of voxels inside body region. Since artifacts are more prevalent in the abdominal compared to chest regions under extremely low dose conditions, we computed RMSEs in both of these regions. We also computed the peak signal-to-noise ratio (PSNR) for regions-of-interest (ROI) evaluation of each reconstruction strategy, in which ROIs were drawn on specific regions such as bone, soft tissue, and lung,

$$\text{PSNR}_{\text{ROI}}(\text{dB}) = 20 \log_{10} \left\{ \frac{N_{\text{ROI}} \times \max(\mu_{\text{ROI}})}{\sum_{j \in \text{ROI}} |\mu_j - \hat{\mu}_j|} \right\}. \quad (23)$$

N_{ROI} is the number of voxel in the corresponding ROI (μ_{ROI}). In (22) and (23), μ_j and $\hat{\mu}_j$ are reconstructions of noise-free (ground-truth image) and noisy data. We computed coefficient of variation on the ROIs defined the ratio of the pixel-to-pixel standard deviation to mean value of a specific ROI. To evaluate the impact of the CTAC on the PET image, all PET images were reconstructed using FBP and the signal-to-noise ratio (SNR) of the three lesions in the reconstructed PET images in Fig. 5(B) was computed as

$$\text{SNR}_{L_i} = \frac{\text{mean}_{L_i} - \text{mean}_{\text{BKG}}}{\text{std}_{\text{BKG}}}, \quad (24)$$

where the signal in the numerator was computed as the difference between average values of the lesion ($L_i \forall i=1,2,3$) and its background (BKG) ROIs of soft tissue or lung. Noise in the denominator was determined by pixel-to-pixel standard deviation (std_{BKG}) of background ROIs. ROIs (37 voxels for each ROI) were drawn on three hot lesions and on their background regions of soft tissue (12 ROIs) and lung (6 ROIs) keeping same size as lesion ROI.

III. Results

A. Attenuation Map Reconstructions under ULD and LD Scans

To evaluate the impact of conventional CT image reconstructions at lower CT dose level, Fig. 5 and 6 compare qualitatively and quantitatively the CT images and CT-based attenuation correction on PET images under dose levels of $I_0 = 2000$ (ULD) and 40000 (LD). Table III summarizes bias and RMSEs in CT sinograms and the reconstructed CT and PET images. All CT images in the left column in Fig. 5 were reconstructed by FBP with a ramp filter. Attenuation-corrected noisy PET sinograms were reconstructed by FBP with a Hanning filter (cutoff frequency of 0.8) on the right column in Fig. 5.

In Table III, The ULD sinogram had 9.7 times higher bias than the LD sinogram. This is likely due to the increase in non-positive sinogram values and subsequent bias added by the combination of the non-positivity correction and the logarithm-conversion operation in (19) which is a non-linear process. The highly biased ULD sinogram values lead to under-estimation indicated by a yellow arrow in the lower part of the reconstructed CT image (Fig. 5(E)) as well as under-correction of attenuation in PET image (Fig. 5(F)). The shadow-like artifacts in ULDCT image affected the PET image, specifically in the posterior region near lesion 2 in as shown in Fig. 5(F). The impact on PET images through CTAC under ULD level is observed in Table III and Fig. 6 as the increased RMSE and coefficient of variations, specifically in posterior region comparing to other regions.

B. Comparison of Attenuation Map Reconstructions of ULD CT Data

Fig. 7 shows the reconstructions of LD (A) and ULD (B to F) CT data. The use of dICD with different penalty functions (E and F) leads to less visual artifacts and noise compared to FBP reconstruction of ULD data (C) and compared to dICD with no regularization (D). The use of the proposed Q- and M- mixture penalty (F) visually has less artifacts and noise than Q-quadratic smoothing alone (E). Also, the combined Q- and M-penalties appear to have slightly biased bone values compared to the FBP and the Q-penalty images, while suppressing more of the banding artifacts in the posterior soft tissue region due to the biased sinogram values from non-positive correction and beam-hardening effect from polychromatic x-ray spectrum. The FBP Hanning low pass filter (FBP-H, C) used a 0.6 cutoff frequency. For these examples, are dICD reconstructions used 10 iterations (We chose 10 iterations to obtain sufficiently converged images.) with different penalty strengths, β and γ , for the Q- and M-penalties. Fig. 7(D) is a weighted least squares reconstruction (equivalent to dICD with $\beta=0$ and $\gamma=0$) followed by Gaussian post-smoothing (WLS-G) with a standard deviation of 0.9 mm. Fig. 7(E) and (F) are dICD reconstructions with a Q-penalty only (dICD-Q with $\beta=5 \times 10^5$ and $\gamma=0$) and with combined Q- and M-penalties (dICD-Q-M with $\beta=5 \times 10^5$ and $\gamma=0.5$), respectively.

Fig. 8 shows attenuation-corrected PET images. Each image in Fig. 8 was corrected with the corresponding attenuation map in Fig. 7. Compared to the PET attenuation-corrected with LD CT image in Fig. 8(A), the FBP reconstructions (B and C) and with WLS-G (D) showed under-correction throughout the posterior regions around lesion 2. The dICD reconstructions with Q- and M-penalties (E and F) showed comparable visual quality with the LD-based attenuation correction (A). Since it is hard to show visually the under-correction of CT-based attenuation in Fig. 8, Fig. 9 compares horizontal profiles of CT-based attenuation and PET images. The profiles were plotted along a horizontal line passing through the posterior region and lesion 2. The profiles of FBP-H (red line) in Fig. 9(A) showed higher bias and cupping-like artifacts due to flipped non-positives and beam-hardening effect at the low dose and the under-correction of attenuation around lesion 2 in (B). The dICD reconstructions with Q- and M-penalties were beneficial compared to FBP methods in reducing the bias in both the CT and PET images.

Fig. 10 provides a quantitative comparison of different CT and PET reconstructions in terms of RMSE inside the body, PSNR of the ROIs on soft tissue, bone, and lung, and SNR related

to the three hot lesions. As shown in Fig. 10(A) for the quantitative comparison of CT reconstructions in Fig. 7, dICD reconstructions reduced RMSE compared with all other reconstructions of ULD data. In terms of ROI-based PSNR (A) and COV (C) analysis in Fig. 10, CT reconstructions using additional noise suppression techniques demonstrated improved performance compared to FBP-R reconstruction of ULD data except bone region. dICD CT reconstruction with Q-and M-penalties resulted in the best PSNR and COV on soft tissue and lung regions, but also had poorer performance than FBP-H in the bone regions. Fig. 10(B) and (C) show the impact of CT attenuation maps on PET reconstruction in terms of RMSE, SNR and COV. The dICD reconstructions resulted in the lowest RMSE compared with all other reconstructions of ULD data and consistently more comparable SNR related to three lesions and COV on the posterior region with the reference FOMs of FBP-R(LD) than the other methods.

IV. Discussion

To control the noise and bias of respiratory phase-matched PET attenuation images calculated from ultra-low dose CT data, we investigated the feasibility of combining quadratic and mixture penalties in a MAP reconstruction framework. We also incorporated the conversion of the energy-dependent attenuation coefficients into the reconstruction step to calculate the 511 keV attenuation images, not in the CT image intensity domain, as a more direct and thus potentially more accurate approach. We simulated polychromatic x-ray spectrum and additive Gaussian electronic noise to generate CT data suffering from beam hardening and other artifacts at low dose levels. We also note that simulation studies are an essential first step in our analysis as it would be challenging to use raw CT data from a clinical system with extreme low-dose levels, considering that commercial systems do not currently operate in this extremely low dose regime.

Decreasing the x-ray intensity by a factor of 20 causes highly biased sinogram values due to non-positivity corrections, which in turn cause biases in the CT and corresponding attenuation-corrected PET images. Robust reconstruction techniques are necessary to control the biases in CT images for very low dose acquisition techniques.

We compared several CT reconstruction techniques, including the standard FBP method, with smoothing filters and iterative reconstruction methods with post-smoothing or penalty functions. For penalty functions, we adopted both a cluster-based mixture penalty and a quadratic smoothing penalty to balance noise from the low-dose scan and resolution loss from the smoothing penalty. All CT iterative reconstruction approaches with penalty functions were more effective in reducing noise and bias in terms of RMSE and PSNR compared to other reconstructions. The combined quadratic and mixture penalties (dICD-Q-M(ULD)) reduced the RMSE by more than a factor 2 compared to post-smoothed iterative reconstruction (WLS-G(ULD)) and FBP with a ramp filter (FBP-R(ULD)). Also, compared to a quadratic penalty (dICD-Q(ULD)), the combined quadratic and mixture penalties produced slightly reduced whole-body RMSE values and slightly increased PSNR values in all regions except for bone. In terms of the impact on PET images, FBP with a Hanning filter under-corrected for attenuation in the posterior region of the PET image. Even though there is only a slight difference between different iterative CT reconstruction techniques, mixed Q

and M-penalties showed an improvement on PET images. We could see that our mixed Q and M-penalty shows a recovery of the cupping artifact due to beam-hardening and non-positivity-corrected sinogram values comparing to FBP with a Hanning filter (FBP-H, red solid line in Fig. 9). The central signal of FBP-H profiles has higher bias than peripheral signals. Iterative reconstruction of one slice took 32 and 40 sec per iteration without and with penalty functions. This computation time could be improved with a more efficient implementation.

The introduction of the M-penalty leads to more hyper-parameters that need to be selected and controlled. The hyperparameters that control the tradeoff between the quadratic and mixture penalty strengths would ideally be adjusted based on the PET imaging task. Methods have been proposed to estimate hyperparameters to improve performance for different tasks [51, 52]. In addition, as discussed above, the M-penalty can introduce local minima because it consists of a combination of two pdfs at each voxel. Alternative methods to encourage convergence to preferred solutions could be applied by applying the M-penalty only after the image is sufficiently converged to the dICD-Q solution. The introduction of the M-penalty leads to a method that is not guaranteed to converge to a global minimum. Specifically, the M-penalty is sensitive to noise and errors in the images; if early iterations incorrectly estimate a voxel, the M-penalty may trap its value in the incorrect cluster. To prevent this, we could turn on the M-penalty during the later iterations of dICD-Q-M and decrease the strength of the Q-penalty during these iterations. These strategies of determining hyper-parameters of Q- and M-penalties would be effective at high noise levels, because the M-penalty at early iterations will be more sensitive to the noise than the signal.

The performance of the mixture penalty depends on the accuracy of the body material histogram. In this study we used a material histogram matched to the scanned object in effort to determine the added value of the M-penalty in a best-case scenario. Methods to obtain material histogram for real whole-body imaging under low dose scans would be needed. Considering that the relative distribution of materials is similar between patients (i.e., the percentage of lung, soft tissue, bone is similar), we hypothesize that this method may work with a common, fixed material histogram that reflects the normal distribution of similar body regions. Further work, however, is needed to test the validity of this hypothesis. The results for different regions in the body had similar pattern of results over the entire body and for different ROIs, so only the summary whole-body results are presented.

We note that in current practice typically CT images are reconstructed with some variant of FBP, converted to 511 keV images that are used for attenuation correction of the PET data, which is then reconstructed with an iterative method. In our study we used iterative methods for the CT data to allow incorporation of more detailed physics models. In addition, we used FBP for the PET data since the intent of this study was to evaluate the impact of the CT reconstruction methods and we wanted a predictable, linear process for the PET images. If the iterative CT methods described here were implemented, it is likely the PET images would be reconstructed with standard iterative methods.

This study introduces a new regularization scheme but does not fully characterize its performance across the multitude of potential clinical scenarios. In brief, performance will

vary at different noise levels, bias artifact levels, and with the CT data. The present results, using a single noise level and a best-case histogram suggest that the mixture penalty does not offer a substantive benefit over conventional quadratic regularization and diminishes enthusiasm for exploring future application of the mixture penalty.

V. Conclusion

For reconstructing PET attenuation maps from ultra-low dose CT acquisitions, the MAP iterative reconstruction method provided lower RMSE and improved the quantitative accuracy of PET attenuation correction over conventional FBP as expected. The quantitative metrics of dICD-Q and dICD-Q-M performance were slightly better than for FBP with low dose data. The combined quadratic and mixture penalties in the MAP framework may provide more flexibility for controlling the tradeoff between bias and variance, although our current study does not suggest a substantive benefit with the combined penalty and these combined penalties require additional hyper-parameter selection.

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Fig. 1. Diagnostic quality CT (A) and near ultra-low dose CT (B) images of same patient; (A) Diagnostic quality CT (100 to 200 mAs, 120 kVp, CTDIvol 10–15 mGy, effective dose 11 mSv), (B) near ultra-low dose CT (5 mAs, 120 kVp, CTDIvol 0.3 mGy, effective dose 0.47 mSv).

Fig. 2. Histograms of CT-based attenuation map values from 4 whole-body PET/CT patients. The histogram shows the distinct peaks of three body regions such as lung, soft tissue, and bone.

Fig. 3. (A) x-ray energy spectrum over 120 energy bins under 120 kVp and energy-dependent attenuation maps of (B) 0.5 and (C) 119.5 keV.

Fig. 4.

(A) Attenuation intensity histogram (blue opened circle), its fitted curve (red solid line) on left y-axis and the normalized pdfs (black solid line) plots on right y-axis for definition of M-penalty function and (B) the mixture pdfs defined in (7) with mixture proportions computed in (17), which are dependent on three different voxel values ($\mu_1=0.001$ (blue), $\mu_2=0.005$ (red), $\mu_3=0.0105$ (black)) for example.

Fig. 5.

Comparison of (left column) CT-based attenuation maps of 511 keV and (right) PET reconstructions under low and ultra-low dose levels (all images are reconstructed by FBP.): (A) and (B) are reference images from noise-free CT and PET data, (C) and (D) from noisy data under $I_0=40000$, and (E) and (F) under $I_0=2000$. (PET data were attenuation-corrected with the corresponding CT images in left column.). Yellow arrows indicates under-estimations in posterior region of CT and PET reconstructions.

Fig. 6. Impact of CTAC on PET images under different levels of $I_0=2000$ (ULD) and 40000 (LD): (A) coefficient variations of soft tissue, bone, lung in CT images, and (B) coefficient variations of background (upper (U) and lower (L) parts of BKG), lung, 3 lesions in PET images.

Fig. 7.

CT-based 511 keV attenuation maps under different levels of $I_0=40000$ (low dose, LD) and 2000 (ultra-low dose, ULD): (A) and (B) are filtered backprojections with ramp (FBP-R) of LD and ULD data, respectively. ULD data were reconstructed by (C) FBP with hanning filter (FBP-H), (D) weighted least square (dICD with $\beta=0$ and $\gamma=0$) followed by Gaussian smoothing (WLS-G), (E) dICD with only quadratic smoothing penalty (dICD-Q, $\beta=5 \times 10^5$ and $\gamma=0$), and (F) dICD with both quadratic and mixture penalties (dICD-Q-M, $\beta=5 \times 10^5$ and $\gamma=0.5$). β and γ are the strength parameters of quadratic and mixture penalties, respectively.

Fig. 8.

Attenuation corrected PET reconstructions from filtered backprojection with hanning filter. Each attenuation map corresponds to different reconstruction techniques under different levels of $I_0=40000$ (low dose, LD) and 2000 (ultra-low dose, ULD): (A) FBP-R-LD, (B) FBP-R-ULD, (C) FBP-H-ULD, (D) WLS-G-ULD, (E) dICD-Q-ULD, and (F) dICD-Q-M-ULD.

Fig. 9. Horizontal profiles passing through bottom region of phantom (the center of Lesion 2 in Fig. 5(B)): (A) CT-based attenuation maps (FBP-H, dICD-Q, and dICD-Q-M) in Fig. 7 under $I_0=2000$ and (B) PET images (Fig. 8) attenuation-corrected by different CT reconstruction in Fig. 8.

Fig. 10.

Performance of reconstruction of ULD data in terms of RMSE, PSNR, SNR, and COV: (A) RMSE on left and PSNR plots on right y-axes of CT images, (B) RMSE on left and SNR plots on right y-axes of PET images, and (C) COV of CT on left and PET images on right y-axes under different levels of $I_0=40000$ (low dose, LD) and 2000 (ultra-low dose, ULD)

TABLE I**Outline of the Direct ICD Reconstruction Algorithm**

Initializes (i) $\hat{\boldsymbol{\mu}}_{511}^{(0)} = \text{FBP}\{\mathbf{g}\}$

$$(ii) \hat{\mathbf{g}}^{(0)} = \text{Fwdprj}\left\{\hat{\boldsymbol{\mu}}_{511}^{(0)}\right\} = \mathbf{D}T_c\left(\hat{\boldsymbol{\mu}}_{511}^{(0)}\right)$$

(iii) Mixture proportions $\{\alpha_{k,j}^{(0)} \mid \forall k \text{ and } j\}$ from $\hat{\boldsymbol{\mu}}_{511}^{(0)}$

for iteration $n=1, \dots, N$

for all voxels in image-space iteration $j=1, \dots, J^a$

 Compute ICD update equation of $E'(x)$

 Find a root of $E'(x)=0$ with a HIS method^b

 Updates (i) $\hat{\boldsymbol{\mu}}_{511;j}^{(n)}$ with the root from the HIS method

$$(ii) \left\{\alpha_{k,j}^{(n)}\right\} \text{ from } \hat{\boldsymbol{\mu}}_{511;j}^{(n)}$$

$$(iii) \hat{\mathbf{g}}^{(n)} = \hat{\mathbf{g}}^{(n-1)} + \mathbf{D} *_j \left[T_c\left(\hat{\boldsymbol{\mu}}_{511;j}^{(n)}\right) - T_c\left(\hat{\boldsymbol{\mu}}_{511;j}^{(n-1)}\right) \right]$$

end

end

^a_jth voxel is chosen in random order.

^b HIS is a half-interval search method to find a root at minimum of the derivative cost function.

TABLE II

Fitted Exponential and Gaussian Functions in Mixture Penalty

Function parameters ^{a,b}	Air (k=1)	Lung (k=2)	Soft Tissue (k=3)	Bone (k=4)
λ or m_k	4906.8 (λ)	0.0025 (m_2)	0.0094 (m_3)	0.0151 (m_4)
σ_k		0.0006 (σ_2)	0.0003 (σ_3)	0.0001 (σ_4)

^aFitted parameters for mixture penalty function in Eq. (8). λ is a parameter of exponential pdf. m_k and σ_k are mean and standard deviation of Gaussian pdf.

^bAll parameters are in mm^{-1} .

TABLE III

Bias and RMSE of CT and PET Reconstructions under Two Noise Levels

I_0	Bias ^a (CT sinogram)	RMSE _{body} ^b (CT images)	RMSE _{body} ^c (PET images) Upper/Lower
40000 (LD)	-0.0028	0.0005	0.3172/0.3219
2000 (ULD)	-0.0272	0.0028	0.3285/0.4062

^aBias was computed in sinogram by Eq. (20).

^bRMSE was computed inside the body in the reconstructed CT images with Eq. (22).

^cRMSEs were computed in the upper and lower halves inside body of the attenuation-corrected PET images.