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Regularized image reconstruction with an anatomically adaptive prior for positron emission tomography

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Abstract

The incorporation of accurately aligned anatomical information as a prior to guide reconstruction and noise regularization in positron emission tomography (PET) has been suggested in many previous studies. However, the advantages of this approach can only be realized if the exact lesion outline is also available. In practice, the anatomical imaging modality may be unable to differentiate between normal and pathological tissues, and thus the edges of lesions seen in the anatomical image may not correspond to functional boundaries in the emission image. In this study, we explored an alternative approach to incorporating an anatomical prior into PET image reconstruction. Of particular interest was the realistic situation where lesions are apparent in the emission images but not in the corresponding anatomical images. In the proposed method, regional information obtained from the anatomical prior was used to estimate an anatomically adaptive anisotropic median-diffusion filtering (AAMDF) prior. This smoothing prior was determined and applied adaptively to each anatomical region on the emission image and then assembled to form a prior image for the next iteration in the reconstruction process. We formulated a two-step joint estimation reconstruction scheme to update the estimated image and prior image iteratively. The proposed AAMDF prior was evaluated and compared with maximum \textit{a posteriori} (MAP) reconstruction methods with and without anatomical side information. In experiments using synthetic and physical phantom data, the AAMDF prior yielded overall higher lesion-to-background contrast and less error in lesion estimation than other algorithms.
for a comparable level of background noise. We conclude that lesion contrast and quantification can be improved using an anatomically derived smoothing prior without requiring knowledge of the lesion boundary. This may have important implications in clinical PET/CT, where lesion boundaries are often not obtainable from CT images.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

Positron emission tomography (PET) is a valuable non-invasive clinical tool for lesion detection and quantitative analysis. However, the utility of PET in practice is often limited by the low spatial resolution and high level of statistical noise relative to signal. Statistical reconstruction algorithms, such as maximum-likelihood expectation maximization (MLEM) (Shepp and Vardi 1982), incorporate a statistical model of the data acquisition process to minimize noise propagation in the reconstructed images. However, since the emission reconstruction problem is ill-conditioned, the reconstructed image is usually very noisy as the algorithm converges towards the maximum-likelihood solution at high iteration numbers (Qi and Leahy 2006).

The ill-conditioning problem can be solved by imposing a priori knowledge as a constraint within a Bayesian reconstruction framework (Qi and Leahy 2006, Green 1990, Alenius and Ruotsalainen 2002). The likelihood function and the regularization prior are combined through Bayes’ rule to form the posterior probability. A maximum a posteriori (MAP) estimate of the image can therefore be found by maximizing the log of the posterior probability. The regularization priors are usually chosen to reflect the property that nuclear medicine images are locally smooth. However, this issue is complicated by the fact that the locally smooth characteristics of radiotracer distribution are often interrupted by sharp transitions due to different tissue structures having different physiological functions; thus one expects to see large radiotracer distribution variation between neighboring tissues and organs (Gindi et al 1993).

The most common regularization prior is the quadratic prior (Gaussian–Markov prior) which smoothes both noise and edge details. However, this prior is unable to differentiate between noise and edges, and thus leads to a blurring of the whole image. One approach to suppressing noise while preserving edges is to incorporate anatomical boundary information to prevent smoothing across organ boundaries (Gindi et al 1993, Lipinski et al 1997, Comtat et al 2002). During the reconstruction, the aligned anatomical images, such as those provided by x-ray computed tomography (CT), supply boundary information for regions assumed to have approximately uniform emission uptake, thus providing a priori information about image smoothness. The advantages of using anatomical information to guide reconstruction and noise regularization have been discussed in many previous studies (Gindi et al 1993, Nuyts et al 2005, Comtat et al 2002, Bruyant et al 2004, Bowsher et al 1996). However, anatomical imaging may be unable to differentiate between normal and pathologic tissues (Vogel et al 2004). It provides no information about the metabolism of organs and lesions and thus lacks sufficient information to guide the reconstruction of functionally abnormal regions, such as lesions, which are remote from anatomical boundaries. Even if anatomical lesion boundaries could be accurately segmented from anatomical images, they do not necessarily coincide with emission boundaries in the PET images. One example is the case of non-small cell lung cancer. Studies have reported that 15–60% of patients exhibit mismatched lesion boundary definitions derived from CT and PET images (Bradley et al 2004, Erdi et al 2002). It has been shown
that the methods using anatomical boundaries to manipulate the weighting of smoothness in MAP reconstruction do not improve lesion detection or estimation accuracy in the absence of accurate lesion outlines, and an inaccurate anatomical boundary may cause artefacts in the final reconstructed image (Comtat et al 2002, Bruyant et al 2004, Kulkarni et al 2007). The effective utilization of prior anatomical knowledge in PET reconstruction without an exact lesion outline is still a significant challenge.

Alternatively, several edge preserving priors (Bouman and Sauer 1993, Lalush and Tsui 1992) have been proposed to produce sharp edges while suppressing noise within boundaries, including the well-known median root prior (MRP) (Alenius and Ruotsalainen 1997, 2002, Chlewicki et al 2004). The MRP is capable of capturing significant edges while encouraging the preservation of locally monotonic images. However, the MRP tends to produce blocky piecewise smoothness or so-called streaking effects (Alenius and Ruotsalainen 2002) in uniform regions, and there is a risk of smoothing out small lesions from the image (Chlewicki et al 2004). In practice, this streaking effect may lead to misinterpretation and poor diagnostic outcomes. Recently, an anisotropic median diffusion filtering (AMDF) (Ling and Bovik 2002) technique, which is a combination of a median filter and the anisotropic diffusion filter (ADF) proposed by Perona and Malik (PM) (1990), has been incorporated into PET image reconstruction (Chan et al 2007, Yan and Yu 2007). The ADF and AMDF are nonlinear iterative filters which are able to remove noise while preserving edge sharpness. The AMDF is specifically intended for removing noise while preserving edges for the relatively low signal-to-noise ratio (SNR) frequently observed in PET images (Ling and Bovik 2002, Luck et al 2005). The incorporation of AMDF in PET reconstruction has been demonstrated, in simulations, to perform better than MRP with regard to noise suppression, edge preservation and reducing piecewise smoothness (Yan and Yu 2007). The edge sensitivity of these filters is controlled by a user-specified edge preserving parameter $K$ which plays an important role in determining whether a part of the image is blurred or preserved. However, the parameter $K$ is usually determined empirically and applied globally to the entire image. Even if $K$ could be optimized for a particular image, it is not clear whether a single value can accurately describe edges or structural features in real images. In practice emission tomographic images usually constitute multiple pathologic features of interest within a single image.

In this study, we investigate a new approach to incorporate an anatomical prior into PET reconstruction with the aim of suppressing noise while preserving the quantitative accuracy of lesions and organ boundaries in the reconstructed image. Of particular interest is the realistic situation where lesions are apparent in the emission images but not in the corresponding anatomical images. For an anatomical prior, we use its organ region information to estimate an anatomically adaptive smoothing prior for the next iteration. With the assumption that the radioactive tracer uptake should be locally smooth within an anatomical compartment, the problem is now reduced to suppressing noise in a locally smooth area while preserving prominent signals, such as those due to lesions. The anisotropic median-diffusion filter is particularly suitable for this problem due to its unique capability for selective smoothing. Simulation and physical phantom studies are performed to evaluate the proposed prior in terms of lesion to background contrast and accuracy of lesion estimation. The proposed anatomically adaptive anisotropic median-diffusion filtering prior (AAMDF) is compared to MAP with a quadratic prior, MAP with a quadratic prior and anatomical boundary information (AMAP), MRP and an AMDF prior. In section 2.1, MAP and MRP methods are introduced. The AMAP approach is described in 2.2. A brief review of the ADF and AMDF is given in sections 2.3 and 2.4. The proposed AAMDF prior is introduced in section 3. Section 4 describes the experiments and quantitative evaluation metrics. The results are given in section 5, and the findings are discussed in section 6.
2. Methods

2.1. Gibbs distribution and priors

A MAP estimate of the image can be computed as the maximizer of the posterior probability

$$\hat{x} = \arg\max_{x \geq 0} L(x) + \ln P(x)$$ (1)

where $\hat{x}$ is the MAP estimate of the radiotracer distribution, $L(x)$ is the log likelihood and $P(x)$ is the prior probability density. Markov random fields are appropriate to model the local homogeneity relationship between neighbouring pixels. A common Bayesian prior is the Gibbs distribution of the form (Geman and Geman 1984)

$$P(x) = \frac{e^{-\beta U(x)}}{Z}$$ (2)

where the hyper-parameter $\beta$ controls the degree of smoothing and $Z$ is a normalizing constant.

$U(x)$ is the Gibbs energy function defined as a sum of potential functions

$$U(x) = \sum_{i=1}^{I} \sum_{m \in N_i} w_{im} V(x_i - x_m)$$ (3)

where $x_i$ is the estimate for a pixel in the image space, the potential function $V(x)$ calculates the intensity difference between pixel $i$ and the neighbouring pixel $m$; $I$ denotes the total number of pixels; $N_i$ denotes the set of nearest neighbours; $w_{im}$ is the weighting factor of neighbouring pixels $i$ and $m$, which is set to 1 for horizontal and vertical neighbours, and $1/\sqrt{2}$ for diagonal neighbours. In this study, the eight nearest neighbours were considered. With the choice of quadratic prior (Geman and Geman 1984), $V(x) = x^2$.

The posterior probability $P(x | y)$ can be maximized by the one-step-late (OSL) iterative procedure proposed by Green (1990), which uses the estimate from the most recent iteration step for $x$ inside the potential function:

$$x_{n+1}^i = \frac{x_n^i}{\sum_j a_{ij} + \beta \sum_j a_{ij} x_n^j} \sum_j a_{ij} y_j$$ (4)

where $a_{ij}$ defines the contribution of image pixel $i$ to projection bin $j$ in the forward projection process and $y_j$ is the acquired projection counts in detector pair $j$. The image is reconstructed by iteratively updating equation (4) to reach at least a local maximum.

The MRP can be incorporated into the OSL formula by replacing the derivative of the prior function with a relative form of the smoothing prior (Alenius and Ruotsalainen 2002)

$$x_{n+1}^i = \frac{x_n^i}{\sum_j a_{ij} + \beta \frac{x_n^i - M_n^i}{M_n^i}} \sum_j a_{ij} y_j$$ (5)

where $M_n^i = \text{Median}(x_n^i, \ i \in N_i)$ is the penalty reference estimated as the median of the image pixels in the neighbourhood $N_i$. A $3 \times 3$ median filter was used in this study. The MRP penalizes deviations of the centre pixel from the median of the neighbourhood rather than the difference between adjacent pixel values. Therefore, the MRP penalizes noise and favours locally monotonic signals.

2.2. Statistical model for including the anatomical prior

The anatomical prior is introduced into the iterative reconstruction procedure based on the assumption that the distribution of radiotracer uptake by PET is locally smooth within a given anatomical region and there may be sharp transitions in the distribution between different tissue...
components. The most common approach for including the anatomical prior is to manipulate the weighting of a smoothing prior (Lipinski et al. 1997, Comtat et al. 2002). For example, the potential function $V(x)$ may be set to zero for neighbouring pixels belonging to different anatomical regions. Thus, no smoothing is applied between these pixels, allowing preservation of any abrupt changes in radiotracer concentration that may occur at organ boundaries. We refer to this model as MAP with anatomical prior (AMAP).

2.3. Anisotropic diffusion filtering (ADF)

Nonlinear ADFs are iterative, ‘tunable’ filters introduced by Perona and Malik (1990). The ADF is formulated as a diffusion process that encourages intra-region smoothing while inhibiting inter-region smoothing. The diffusion process is defined as the divergence (div) of the product of a diffusion equation and the image gradient

$$\frac{\partial x}{\partial t} = \text{div}[C(\nabla x) \cdot \nabla x] \quad (6)$$

where $x$ is the image, $t$ is the iteration step, $\nabla x$ is the local image gradient and $C(\nabla x)$ is the diffusion function, which is a monotonically decreasing function of the image gradient magnitude, sometimes called the ‘edge-preserving’ function. The diffusion process is tuned to return large values in the regions with no or small intensity fluctuations and small values in the areas with large intensity variations. This leads to conditional smoothing which encourages intra-region smoothing while preserving the sharp transition between two different regions.

The following diffusion functions were proposed by Perona and Malik (1990):

$$C_1(\nabla x) = \frac{1}{1 + (\frac{\nabla x}{K})^a}, \quad a > 1 \quad (7)$$

$$C_2(\nabla x) = \exp[-(\frac{\nabla x}{K})^2] \quad (8)$$

where $K$ is the edge preserving parameter which can be tuned for a particular application. It is a user-specified constant which determines the threshold of the local gradients and controls the edge sensitivity of the filter. To better clarify the diffusion process and the effect of $K$, it is also convenient to define a flow function as

$$\Phi(\nabla x) = C(\nabla x) \cdot \nabla x. \quad (9)$$

With the flow function, the discrete formulation of (6) can be written as

$$x(t + 1) = x(t) + \frac{\lambda}{N_i} \sum_{m \in N_i} \frac{1}{(w_{i,m})^2} \Phi(w_{i,m} \nabla x_{i,m}(t)) \quad (10)$$

where $\nabla x_{i,m} = x_i - x_m$ is the gradient of the intensity of pixel $i$ at the $t$th diffusion process with respect to the neighbouring pixel $m$, $N_i$ is the number of neighbours of pixel $i$ (eight neighbours are considered in this study), and $\lambda \in [0, 1]$ controls the rate of diffusion. This parameter is usually set sufficiently small to avoid destabilizing the diffusion process, and $w_{i,m}$ is the weight between neighbouring pixels such as $1$ for vertical and horizontal neighbours and $\sqrt{2}$ for diagonal neighbours.

The flow functions of $C_1$ and $C_2$ are plotted in figure 1. It can be observed that the flow function increases monotonically from zero, reaches a peak, and then asymptotically decreases to zero. The greatest flow value is produced when the image gradient magnitude is close to the value of $K$, such as $K_1$ and $K_2$ shown in figure 1, and little flow is produced when the gradient
magnitude is much smaller or much bigger than the value of $K$. This implies that by choosing $K$ to correspond to the image gradients due to noise, the noise can be preferentially smoothed while large image gradients due to edges are preserved because the flow is small. The flow function of $C_1$ with $a = 2$ possesses a wider peak which favours smoothing a wider range of gradient magnitudes while $C_2$ favours high-contrast edges over low-contrast ones (Perona and Malik 1990). Since our purpose is to preserve a prominent signal in a homogeneous area, such as a focal lesion within a single anatomical region, $C_2$ is more suitable for our application. However, we noted that by setting $a = 4$ in $C_1$, it actually yields a similar flow function as $C_2$ (figure 1). Therefore, $C_1$ with $a = 4$ was used in this study as it is more computationally efficient.

Selecting an accurate value of the diffusion constant $K$ for a noisy image is critical for the performance of the ADF. However, $K$ is very sensitive to the image geometry and noise in the image. Different choices of $K$ give quite different results. In the Perona and Malik (PM) model (Perona and Malik 1990), $K$ was calculated as the ‘noise estimator’ described by Canny (1986). This method is not applicable in emission tomographic imaging due to the non-stationarity of the noise, i.e. the noise level varies across the image (Barrett et al 1994, Wang and Gindi 1997). Using a constant threshold prevents adaptation to this variation in noise. Several studies have proposed various modifications of the PM model to reduce the sensitivity of the ADF to the selection of the parameter $K$. For example, Whitaker (Whitaker and Pizer 1993) proposed determining $K$ from the gradients at each pixel in the image and Li and Chen’s paper (Li and Chen 1994) proposed setting $K$ as a decreasing function of the evolution number instead of using a fixed value of $K$ during the process of diffusion. However, all the above methods may fail to yield satisfactory results in low SNR images where the gradient magnitude due to noise may compete with or exceed the edge response.

2.4. Anisotropic median-diffusion filtering (AMDF)

Recently, a modified ADF which is particularly suitable for the low SNR environment of molecular imaging was proposed by Ling and Bovik (2002). They suggested using a median filter in combination with a small $K$ in the diffusion process. Within each iteration step of the diffusion process, areas having small gradient are smoothed, while areas having a large gradient relative to the surrounding areas are left unchanged. A median operation is used to
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remove large noise spikes after diffusion. With the addition of the median filter, the AMDF is relatively insensitive to the exact value of $K$. This approach has recently been applied in PET reconstruction (Yan and Yu 2007) and shown good noise suppression together with edge preservation on piecewise smooth simulations. However, no general strategy was proposed to determine how small the parameter $K$ should be in the above studies. The parameter was determined empirically and was application dependent. With an improper selection of $K$, the AMDF prior tends to break the wide smooth edges into many discrete steps, the so-called staircasing effect, and smooth out low contrast features (Whitaker and Pizer 1993). This is particularly challenging for PET imaging due to the complicated situation of non-stationary noise, multiple gradient magnitude (organ boundaries and lesions), low SNR and the highly undesired staircasing effect. These effects were also observed in all our experiments described below. In this work, the AMDF was incorporated into reconstruction by replacing the median process $M_i$ in equation (12), similar to the approach in Yan and Yu (2007).

3. Anatomically based anisotropic median-diffusion filtering (AAMDF)

3.1. Inclusion of anatomical information

We present a new approach to incorporate an anatomical prior into PET reconstruction. The method involves two ways of using anatomical information; the organ boundary definition is used to influence the estimation of emission values in close proximity to the boundaries, while the organ region information is used to estimate an anatomically adaptive smoothing prior for the next iteration. By assuming that the radioactivity uptake is locally smooth within an anatomical region, the problem now is reduced to suppressing noise while preserving prominent signals, such as lesions. The AMDF is particularly suitable for this problem due to its unique attribute of applying selective smoothing.

In the proposed method, the anatomical image is segmented into $C$ classes of regions representing different anatomical regions which are assigned to the pixels on the current estimate of the emission image. An example with $C = 3$ could be $c = 1$ for pixels inside the lung region, $c = 2$ for soft tissues and $c = 3$ for outside the body. Each pixel on the emission image is assigned to a mutually exclusive class representing an anatomical region similar to Comtat et al (2002). Since the radiotracer concentration is locally smooth within a single anatomical region, the small fluctuation in this region could be reasonably assumed to be mainly caused by noise. Thus, the edge preserving parameter $K$ could be determined in proportion to the local standard deviation of the PET intensity values within each anatomical region on the emission image. In order to more accurately estimate the intensity fluctuations caused by noise, the maximum and minimum 10% of the intensity values are considered as outliers and discarded in calculating the regional standard deviation. This is to prevent the case where a large lesion resides in a relatively small anatomical region, causing bias in the standard deviation estimation. As suggested by Ling and Bovik (2002), the AMDF is fairly insensitive to the selection of $K$ if $K$ is small. In our experiments, we found that if $K$ is too small compared to the local standard deviation, the resultant image appears similar to the MRP reconstruction with streaking effects in the uniform regions. Therefore, we empirically selected $K$ as 70% of the local standard deviation of a single organ region. Thus, the parameter $K$ is relatively small within each organ region. Indeed, as can be observed from figure 1, the flow function increases rapidly on the left side of the peak and then gradually approaches zero on the right side of the peak. Thus, a slight shift of $K$ to the left is expected to be more robust to the estimation accuracy of the parameter $K$. 
In contrast to conventional ADF and AMDF where \( K \) is selected as a constant for the whole image and throughout the filtering process, in this study \( C \) different values of \( K_c \) were calculated adaptively for each anatomical region at each iteration \( n \). As the image is gradually formed and regularized during the reconstruction process, we expect the \( K_c \) to fluctuate at the beginning and converge towards a constant value as the reconstruction proceeds.

### 3.2. Two-step joint estimation reconstruction scheme

Since the \( K_c \) values are determined from the previous estimation of \( x^n_c \), we formulate the following alternating two-step updating estimation scheme during each reconstruction iteration.

**Step 1. \( K_c \) update and anisotropic median-diffusion filtering**

\[
K^n_c(x^n_c) = 0.7 \times \sigma (x^n_c) \tag{11}
\]

where \( \sigma (x^n_c) \) is the standard deviation in region \( c \) of image \( x \) on the \( n \)th iteration. Substituting the regional and iteration-dependent \( K^n_c \) in the anisotropic median-diffusion process (10), we obtain

\[
x^n_{i,c}(t + 1) = x^n_{i,c}(t) + \frac{\lambda}{N_i} \sum_{m \in N_i} \Phi (\nabla x^n_{i,m,c}(t), K^n_c) \tag{12}
\]

where \( \nabla x^n_{i,m,c} = x^n_{i,c} - x^n_{m,c} \) is the gradient of the intensity of pixel \( i \) at the \( n \)th iteration in the reconstruction process with respect to the neighbouring pixel \( m \) within anatomical region \( c \), and \( \lambda \) is set to 1/7 in this case as eight neighbouring pixels are considered (Gerig et al. 1992). The parameter \( t \) is set to 5 which implies that on the \( n \)th reconstruction iteration, five iterations of the AMDF process are applied. Note that in any anatomical region \( K_c \) is invariant during the filtering process and variant during the reconstruction iteration. The diffusion function shown in equation (7) is used. Each anatomical region is smoothed independently and forms a regionally adaptive prior. For example, for the lung region, those pixels that do not belong to lung regions are set to zero. In our implementation, the initial image in the reconstruction is chosen as a uniform image without intensity variation; therefore, \( K_c \) is assigned with an initial value of 0.5 for the first iteration in all regions. All the regionally adaptive smoothed regions are then combined to form a prior:

\[
A^n = \sum_{c=1}^{C} x^n_c. \tag{13}
\]

After the diffusion process, a follow-up median filter is applied to the combined prior term:

\[
\hat{A}^n = \text{Median}(A^n, W) \tag{14}
\]

where \( W \) is the window for the median operator (such as a 3 × 3 square) and the filtered image is used as a prior for the estimate in the next reconstruction iteration.

**Step 2. Image update**

The prior is then incorporated into equation (5) by replacing the median prior \( M_i \), with the AAMDF prior \( \hat{A}^n \) as shown below:

\[
x^n_{i+1} = \frac{\hat{A}^n}{\sum_j a_{ij} + \rho \sum_j a_{ij} \hat{A}^n_j} \sum_j \frac{a_{ij} y_j}{\hat{A}^n_j} x^n_{j}. \tag{15}
\]

Similar to MRP, \( \hat{A}^n \) is a relative form of the smoothing prior which depends on the estimate from the previous iteration rather than the difference between adjacent pixel values. The
difference is that in MRP, the value of each image pixel is drawn towards its own local median. However, the median filter is known to be less effective at removing Gaussian and Poisson noise. Instead, in AAMDF, each image pixel is attracted to its local median on the image resulting from the ADF process. This selective smoothing filter suppresses most pixel gradients corresponding to noise and spares the gradients corresponding to edges. Thus, the local median is a more accurate estimate of the locally monotonic patch.

The proposed smoothing prior term is a combination of individually smoothed organ regions; therefore, the abrupt changes between organs are naturally retained in the reconstructed images. The incorporation of anatomical boundary information in AAMDF could be considered as indirect since the prior penalizes the differences between pixels $x_i$ and component $A_i$. This is different to AMAP where the potential function of adjacent pixels belonging to different anatomical regions is set to zero, which results in a sharper anatomical boundary. The differences between these two approaches will be further elaborated in section 6 based on the experimental results.

As the AAMDF prior is a relative smoothing term, there is no explicit prior function $P(x)$ defined due to the difficulties of involving the anisotropic-median diffusion process. However, the anisotropic median-diffusion filter is interesting due to its ability to selectively smooth low SNR images.

4. Simulations and experimental study

4.1. Simulation study 1: disc phantom

The proposed AAMDF prior was first evaluated by applying it to a computer-simulated disc phantom. This allowed evaluation of the AMDF and AAMDF priors with lesions of different contrasts, and the effect of different combinations of $\beta$ and $K$ on reconstructed image properties. The 2D $128 \times 128$ pixel disc phantom is shown in figure 2(a). The pixel size was 0.406 cm. The object consisted of a uniform activity disc background with four $5 \times 5$ pixel lesions. Lesion 1 was a cold lesion with lesion to background ratio of 0.5:1; lesions 2, 3 and 4 were hot lesions having contrast levels of 1.5, 2 and 2.5 relative to the background, respectively. The disc had uniform attenuation coefficient simulating soft tissue at 511 keV ($0.095 \text{ cm}^{-1}$).
The simulated activity was forward-projected to produce a sinogram comprising 64 angular projections each containing 128 linear samples. To account for the finite resolution of the detector, the one-dimensional projections were blurred by convolving them with a Gaussian filter with full width at half maximum (FWHM) of 0.6 cm. Poisson noise was added to the emission sinogram which had 850 K total counts. The emission data were corrected for attenuation before reconstruction and all images were reconstructed using the same system matrix that was used for computing the projections.

**4.2. Simulation study 2: thorax phantom**

An emission scan of a digital phantom resembling the human thorax was simulated (figure 2(b)). The body (soft tissue) and lung regions had attenuation coefficients of 0.095 cm$^{-1}$ and 0.03 cm$^{-1}$ (Meikle *et al.* 1994), respectively. Three $3 \times 3$ lesions were inserted into the phantom: lesions 1 and 3 were placed within the soft tissue region and lesion 2 was placed within the left lung. The phantom without lesions was used as the anatomical prior as shown in figure 2(c). No correlated lesion outlines were available in the corresponding anatomical prior. This represented the realistic case where the local variations in tracer uptake may not correspond to changes in the anatomical image. Lesions were simulated with smaller size than the disc phantom to analyse the effect of the edge preserving priors on small target signals. Lesion 3 was placed in close proximity to the lung boundary to evaluate the effect of staircasing, which may result from the AMDF prior, on lesion detection and accuracy of estimation within the lesion region of interest (ROI). The relative activity concentrations of lesion:soft tissue:lung were 4:2:1. The object was forward projected and blurred with the same procedure as that applied to the disc simulation. The total number of counts in the sinogram was 950 K. In order to perform a thorough quantitative analysis of the proposed method, we simulated 100 realizations with Poisson noise added.

**4.3. Physical phantom studies**

A physical torso phantom (Elliptical Lung-Spine Body Phantom™, Data Spectrum Inc., Hillsborough, NC) was used to further assess the performance of the proposed algorithm as shown in figure 3. CT and $^{18}$FDG PET scans of the torso phantom were acquired on a Siemens Biograph Truepoint PET/CT scanner (Siemens Medical Solutions, Hoffman Estates, IL). The fillable volumes of the phantom and the lung inserts which contained Styrofoam beads were 10 L and 0.7 L, respectively. Three 4.5 mL hot lesions contained in plastic tubes approximately 10 mm in diameter and 50 mm in length were placed in locations corresponding to the lesions in the computer simulation. The phantom contained a total of 213 MBq of $^{18}$FDG. The FDG concentrations in the lesions and lung tissue were 4 and 0.5 times the soft tissue concentration, respectively.

PET data were acquired for 4 min. The sinogram consisted of 168 radial samples and 168 angular samples. For the PET scan, the true and random event rates were approximately 480 kcps and 175 kcps, respectively. The acquired sinogram was normalized, corrected for attenuation and scatter, and rebinned to 2D using Fourier rebinning (FORE) (Defrise *et al.* 1997).

The anatomical prior for AMAP and AAMDF was obtained by segmenting the CT image by thresholding. The lesions (1 and 3) residing in the soft tissue region were not detected in the CT image. Therefore, only lesion 2, in the lung region, could be segmented. This simulates a realistic scenario where lesions are apparent in the emission images but not in anatomical images. The 27th CT slice and its segmentation, which was used as the anatomical prior to
reconstruct the corresponding slice of the PET image with AMAP and AAMDF, are illustrated in figures 3(a) and (b), respectively. Note that the beads were unevenly distributed in the left lung region which may cause the activity within this region to vary gradually. This simulates a realistic situation where radioactivity update distribution may not be locally uniform within a single anatomical organ. The CT image was resampled to match the pixel size of the PET image. The boundary of lesion 2 appears square due to linear interpolation applied during the resampling. The tenth plane of the physical phantom is shown in figure 3(c) where the caps of the tubes used to simulate lesions can be observed to reveal the true lesion locations.

4.4. Reconstructions and numerical evaluations

All the computer simulations and the physical phantom were reconstructed with MAP, MRP, AMDF and AAMDF priors. The thorax simulation and physical phantom images were also reconstructed with AMAP to evaluate the efficacy of using anatomical boundary information in the reconstruction. The quadratic function was used as the potential function for MAP and AMAP. Since the MRP has been widely evaluated due to its well-known characteristic of suppressing noise while preserving edges, we included this method to evaluate the edge preserving ability of the proposed method. All reconstruction methods were accelerated with the ordered subsets method (Hudson and Larkin 1994) with 8 subsets and 40 iterations, which is approximately equivalent to 320 iterations.

Quantitative evaluations of the 100 noise realizations were made using lesion to background contrast and normalized root mean square error (NRMSE) as the figures of merit (FOM). The location and size of the lesion ROIs were defined to coincide with the true lesions as shown in figure 2(b). The ROIs used to calculate the background standard deviation were defined in the soft tissue region and lung region for lesions 1, 3 and 2, respectively, as illustrated in figure 2(b) (the regions surrounded by the dashed lines).

The lesion to background contrast was defined as

\[
\text{Contrast} = \frac{|M_l - M_r^B|}{M_r^B}
\]  

(16)
Figure 4. Reconstructed images with (a) MAP, $\beta = 0.06$; (b) MRP, $\beta = 0.4$; (c) AMDF, $K = 0.5$, $\beta = 0.4$; (d) AMDF, $K = 1$, $\beta = 0.4$; (e) AMDF, $K = 2$, $\beta = 0.4$; (f) AAMDF, $\beta = 0.4$. All images are scaled to the same maximum pixel value with comparable background variance.

where $M_l^l$ and $M_l^B$ denote the mean intensity value within the lesion $l$ and the mean intensity value within the background ROI of noise realization $r$, respectively. The average contrast was plotted versus average standard deviation of the background ROI across 100 noise realizations.

The normalized root mean square error (NRMSE) was defined as

$$d_l = \frac{1}{t_m} \sqrt{\frac{1}{R} \frac{1}{N_l} \sum_{r=1}^{R} \sum_{k \in N_l} (x_{r,k} - t_l)^2}$$

where $t_l$ is the true pixel intensity within an ROI $l$, $t_m$ is the mean of $t_l$, $N_l$ is the number of pixels within the ROI and $R$ is the number of noise realizations. The NRMSE measured inside the entire disc phantom was first plotted against the iteration number to evaluate the accuracy and convergence towards the true phantom for the disc simulation. To evaluate the estimation accuracy, the lesion NRMSEs were plotted against the background NRMSE for the thorax simulations with multiple noise realizations.

5. Results

The reconstructed images of the disc phantom are shown in figure 4. All images were scaled to the same greyscale as the true image shown in figure 2(a). The penalty parameter $\beta$ was chosen in such a way that the standard deviation in the background regions (the region surrounded by the dashed lines) was approximately the same. Thus, the algorithms were ‘balanced’ with respect to $\beta$. We observed that MAP with quadratic prior smoothed out
Figure 5. Errors in disc simulation reconstructions as a function of the smoothing parameter. NRMSE of lesion versus NRMSE of background for (a) AMDF with $K = 0.4$–2 and AAMDF, and (b) MAP, MRP, AMDF with $K = 1.6$ and 2, and AAMDF.

noise and lesions simultaneously. The MRP was more effective than MAP at smoothing out noise while preserving lesions. However, it also produced blocky piecewise smooth regions (streaking effect) in the background region. For the AMDF prior, three images shown were reconstructed with different $K$ values and a single $\beta$. With a small $K$ value, such as $K = 0.5$, the resultant image appeared similar to the image reconstructed with MRP. This was because with a small $K$ value, the anisotropic diffusion filtering process did not smooth out the noise effectively and the reconstruction was dominated by the follow-up median prior. The image became smoother when $K$ was increased to 1. However, when $K$ was further increased to 2, the AMDF prior tended to smooth out the cold lesion ($L_1$) and lesion that had low contrast ($L_2$) as illustrated in figure 2(e). These results demonstrate that the AMDF method is very sensitive to the selection of the parameter $K$ where a small variation in $K$ will lead to a large variation in the final results. AAMDF automatically estimated parameter $K$ during each iteration which produced a smooth background and all lesions were effectively preserved.

In order to further illustrate the relationship between the parameter $K$ and $\beta$ for AMDF, the NRMSE of the lesion versus NRMSE of the background for a single noise realization is presented in figure 5. Each curve was obtained by varying the smoothing parameter $\beta$. The performance of AMDF varied significantly with different $K$ values. Small $K$ values (0.4 and 0.8) did not suppress noise effectively whereas large $K$ values (e.g. 2) were very sensitive to the selection of $\beta$. AAMDF performed similarly to AMDF with $K = 1.6$, which shows lower NRMSE in the lesion for a comparable level of NRMSE in the background than other methods. It demonstrates that AAMDF with an automatically determined $K$ value yielded similar results to the AMDF prior with an optimized $K$ value.

The analysis of convergence with the proposed method is presented in figure 6. The OSEM reconstructed image continued to deteriorate with increasing iterations while all other methods using a prior term converged to a stable solution. To illustrate the variation of $K$ during reconstruction, we plotted $K$ against the iteration number for several $\beta$ values as shown in figure 7. The parameter $K$ started at 0.5 and rapidly increased before peaking at about the tenth iteration. This is because the estimation tended to match the measured noisy projections. As the reconstruction continued to evolve with increasing iterations, the noise in the image was regularized by the AAMDF prior and the parameter $K$ decreased again before converging to a constant at about the 100th iteration. In fact, several studies have suggested that this parameter should be scaled during the filtering process, for example as a decreasing function
Figure 6. NRMSE versus the number of iterations for all the algorithms. The numbers 0.02–0.9 in (a) correspond to the $\beta$ values. The first number for AMDF in (b) is the value of $\beta$ whereas the second parameter indicates $K$.

Figure 7. The automatically estimated edge preserving parameter $K$ from AAMDF reconstruction is plotted as a function of the iteration number for different $\beta$ values.

of the iteration number of the filtering process (Li and Chen 1994, Whitaker and Pizer 1993, Monteil and Beghdadi 1999). Increasing $\beta$ resulted in stronger smoothing, and smaller $K$ values were obtained. This implies that the parameter $K$ is inversely related to $\beta$.

Figure 8 shows one representative sample of the 100 noise realizations of the thorax simulation. All reconstructed images shown were scaled to the same maximum pixel value as the true image shown in figure 2(b). The images in figures 8(a) and (b) show that MAP and AMAP yielded visually similar lesion to background contrast for lesions 1 and 2. The incorporation of anatomical boundaries in AMAP aided the localization of lesion 3. A visual comparison suggests that the MRP in figure 8(c) performed better in suppressing noise than the quadratic prior used in MAP and AMAP, and yielded higher lesion to background contrast. However, the inaccurately formed boundaries, such as in the lungs, and the streaking effect in the uniform background may be disturbing to a human observer during image interpretation. Images reconstructed with AMDF with two $K$ values are shown in figures 8(d) and (e). These two values were obtained by trial and error within the range of 0.1–2, based on the criteria of
noise reduction while yielding higher lesion contrast by visual assessment. Similar to MRP, the AMDF method broke the organ boundaries into many discrete steps (staircasing effect). With the aid of the anatomical prior and adaptively estimated parameter $K$, the AAMDF prior effectively reduced the noise and the staircasing effect while preserving all the lesions. The proposed method demonstrated superior visual quality compared with the other algorithms.

Figure 9 is a plot of $K$ as a function of the iteration number for several $\beta$ values for the thorax simulation. We observed that $K$ converged to different values in different anatomical regions. In the lung region, the value of $K$ gradually increased and stabilized at about 100
Table 1. Mean and standard deviation of the automatically estimated $K$ from 100 to 320 iterations for the disc and thorax simulations.

<table>
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<tr>
<th>Beta</th>
<th>Mean</th>
<th>Standard deviation (%)</th>
<th>Mean</th>
<th>Standard deviation (%)</th>
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<th>Standard deviation (%)</th>
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<tr>
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<td>0.79</td>
<td>1.08</td>
<td>1.01</td>
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<td>0.49</td>
</tr>
<tr>
<td>0.30</td>
<td>2.32</td>
<td>1.27</td>
<td>0.93</td>
<td>1.34</td>
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<td>0.47</td>
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</table>

iterations. The behaviour of $K$ in the soft tissue region is similar to that obtained in the disc simulation (figure 7). A summary of the mean and standard deviation of $K$ from 150 to 320 iterations for the disc and thorax simulations is shown in table 1. Interestingly, the automatically estimated $K$ values from AAMDF in two different organ regions are somewhat close to our experimentally selected $K$ values for the AMDF prior, which yielded better results based on visual assessment than other $K$ values within the selection range. For example, when $\beta$ was equal to 0.12, the means of the estimated $K$ values in the soft tissue and the lung regions were 2.05 and 1.21, respectively (table 1). Lesions 1 and 3 in the AAMDF reconstructed image (figure 8(f)) appear similar to the corresponding lesions in the AMDF reconstructed image with $K = 1.6$ (figure 8(e)); and lesion 2 appears similar to the image reconstructed with AMDF with $K = 1$ (figure 8(d)). These results support the argument that $K$ should be set adaptively for each anatomical region. In addition, it can also be observed from figure 9 that $K$ fluctuates more in relatively nosier regions, such as the lung, than in soft tissue regions.

Figure 10 presents plots of the average lesion contrast versus the average background standard deviation for all lesion locations using 100 noise realizations. For lesions 1 and 2, as expected, MAP and AMAP demonstrated almost the same performance because the same regularization was applied to these two lesions. AMAP yielded the highest contrast for lesion 3 among all the algorithms as the anatomical boundary excluded pixels located in the lung region from contributing to pixels within lesion 3. The MRP demonstrated improved lesion contrast compared to MAP. The AAMDF prior yielded the highest lesion to background contrast for lesions 1 and 2 and was slightly inferior to AMAP for lesion 3. The AMDF prior with both $K$ values yielded curves that lay between those of the AAMDF prior and MAP, where parameter $K = 1.6$ resulted in better performance than $K = 1$.

Figure 11 presents the NRMSE values of the lesion regions versus the NRMSE of the background regions for all the reconstruction algorithms. The curve for each algorithm was obtained by varying the smoothness parameter $\beta$. Data points that are close to the origin provide better performance in terms of this FOM which means more accurate lesion estimation with less variance in the background. Similar to the lesion contrast evaluation, the NRMSE curves for MAP and AMAP suggest similar performance for all lesions except lesion 3, for which AMAP demonstrated superior performance than all other algorithms. The MRP algorithm yielded NRMSE curves between MAP and AMDF type priors for all the lesion locations, and the AMDF prior with $K = 1.6$ performed better than $K = 1$. Overall, the proposed AAMDF prior yielded lower NRMSE than other algorithms for a comparable level of background noise for all lesions except lesion 3, where AMAP demonstrated better performance.
Figure 12 shows reconstructions of the 27th plane of the physical thorax phantom for all algorithms. The OSEM reconstructed image post-filtered with a $5 \times 5$ Gaussian filter with FWHM of 3 pixels (OSEM-F) is shown in figure 12(a) as a reference image. Similar to the thorax simulation, the image reconstructed with AMAP in figure 12(c) demonstrates sharper transitions between neighbouring anatomical structures in contrast to the blurred boundary produced in the image reconstructed with MAP as shown in figure 12(b). However, the shape of lesion 2 in the AMAP image suggests that the anatomical lesion outline excessively influenced the final reconstruction. This illustrates the problem that an imperfect anatomical prior may cause an artefact in the reconstructed image. The image reconstructed with MRP shown in figure 12(d) demonstrates slightly better noise suppression and preservation of lesion contrast than the images reconstructed with MAP and AMAP. The edge preserving parameter $K$ for the AMDF prior was selected empirically within the range 0.01–0.2 by visually assessing the lesion to background contrast. The parameter $K = 0.06$, which yielded the best visual quality is shown in figure 12(e). Although the AMDF prior suppressed noise effectively, a single global parameter $K$ is unable to preserve all the edges. We observed that part of the lung boundaries and lesion 2 were also smoothed out.

The image reconstructed with the AAMDF prior (figure 12(f)) illustrates the ability of this algorithm to achieve high lesion to background contrast as well as relatively low noise in the background. As with AMAP, inclusion of the anatomical prior produced a sharp and accurate organ boundary definition. Lesion 2 in the image reconstructed with the AAMDF prior demonstrates more physiologically realistic lesion appearance than the rectangular shape produced by AMAP. This is because those pixels belonging to lesion 2 but not bounded in the anatomical lesion outlines were considered as edges and the involvement of the neighbourhood
Figure 11. Lesion NRMSE versus background NRMSE across 100 noise realizations for all lesion locations.

Figure 12. The physical thorax phantom: images reconstructed with (a) OSEM-F; (b) MAP, $\beta = 0.02$; (c) AMAP, $\beta = 0.02$; (d) MRP, $\beta = 0.2$; (e) AMDF, $k = 0.06, \beta = 0.12$; (f) AAMDF, $\beta = 0.12$. All images are displayed in the same greyscale.
lung pixels in smoothing was reduced to avoid edge blurring. As a consequence, the outline of lesion 2 in the image reconstructed with the AAMDF prior is similar to the reconstruction without lesion outlines. Thus, the AAMDF prior appears to be more robust to imperfect anatomical priors than AMAP.

6. Discussion and conclusions

A new approach for incorporating anatomical prior information into PET reconstruction was proposed that improved lesion contrast and quantification without specifically requiring knowledge of the lesion boundary. In contrast to AMAP, the proposed approach uses the anatomical information in two separate ways: the anatomical boundary definition is used to influence the estimation of emission values in proximity to the boundaries in the PET image, while the organ region information is used to estimate an anatomically adaptive anisotropic median-diffusion filter to generate a smoothing prior for the next iteration in the reconstruction process. The image is updated in a two-step joint estimation process. In the first step, the edge preserving parameter $K$ is estimated adaptively based on the local statistics within each organ region on the previous image estimate. The labelled anatomical regions of the PET estimation are separately smoothed with the anisotropic median-diffusion filter using the estimated parameter $K$. All the smoothed regions are then assembled to form a prior image for the second step to update the image estimate.

Due to the limitations imposed on spatial resolution and signal-to-noise ratio in PET, one of the major challenges in PET image reconstruction is to suppress noise in the background while preserving useful features, such as edges and lesions. Our experiments demonstrate that the conventional incorporation of anatomical boundaries with MAP reconstruction does not improve contrast or estimation accuracy in the lesion ROIs, unless the lesion outline is available as part of the prior, or it lies in close proximity to another anatomical boundary. However, our physical phantom study also revealed that a mismatch between anatomical and functional images causes artefacts in the reconstructed image.

An alternative approach to preserve edges, using edge-preserving priors such as MRP and AMDF, was also explored in this study. Quantitative evaluations showed that the MRP only achieved superior performance for a high contrast lesion (lesion 2 in the thorax simulation); it performed similarly to the quadratic prior for low contrast lesions, which agrees with results presented in Chlewicki et al (2004). In all experiments, the AMDM prior with optimal values of the parameters $\beta$ and $K$ performed better than both MAP and MRP. However, a small change in $K$ caused large differences in the final reconstruction results. There is also a danger that use of a single scalar $K$ value may smooth out useful features such as the lesion and organ boundaries as shown in figure 12(e). In addition, MRP and AMDM tend to cause stepwise smoothness in the gradually varying regions, such as organ boundaries (figures 8(d) and (e)) and the lung regions of the physical phantom (figures 12(d) and (e)).

The aforementioned difficulties were solved by combining the anatomical prior and AMDF. The anatomical prior allowed the parameter $K$ to be estimated automatically with local statistics. The AMDM prior was applied adaptively to each organ region and suppressed noise and preserved lesions effectively without requiring an accurate anatomical lesion outline. Compared to MRP and AMDF, AAMDF also reduced the stepwise smoothness as can be observed in the thorax simulation and the physical phantom study. In addition, unlike other edge-preserving priors, which usually require a user-specified parameter in addition to the smoothing parameter, the AAMDF prior requires only one parameter ($\beta$) to be specified. This significantly simplifies optimization of image quality.
AAMDF demonstrated superior performance in the quantitative evaluations except for lesion 3, where AMAP yielded better performance. This is due to the difference in approach of these two algorithms to incorporating anatomical boundary information. Unlike other lesions, lesion 3 was immediately adjacent to the lung boundary. Thus, the lung boundary in the anatomical prior acted as a half lesion outline, which could be considered a semi-perfect lesion outline. For AMAP, no smoothing was applied between the neighbouring pixels residing in different anatomical regions which resulted in a sharp anatomical boundary. Therefore, lesion 3 totally avoided the influence of neighbouring pixels in the lung region. In contrast, the AAMDF incorporated anatomical boundary information indirectly since it penalized the differences between the object pixel and a relative smoothing prior term which was a combination of regionally adaptive smoothing priors for each organ region. Thus, the contribution from the neighbouring pixels in the lung region was not totally turned off. Although AMAP performed better in the quantitative evaluations on lesion 3 of the simulation data, the physical phantom study revealed that this indirect way of incorporating the anatomical prior is more robust to mismatch of anatomical and functional images than the AMAP algorithm. With the same anatomical lesion outline included, AMAP (figure 12(c)) excessively influenced the final reconstruction and caused an artefactual square shape for lesion 2 in the reconstructed image, whereas AAMDF was not affected by the artefactual lesion outline in the anatomical prior. The robustness of AAMDF to mismatches between anatomical and functional images will be further investigated in future work.

In this study, the AAMDF prior was incorporated into the OSL framework in a similar manner to the MRP implementation. However, the approach of including a smoothed image as a prior for the next iteration in the OSL framework is a heuristic approach which lacks a defined objective function. Therefore, formula (14) is not guaranteed to converge to a global maximum. However, in our experiments, we observed that the algorithm always converged to stable solution. Nevertheless, we are particularly interested in exploring a new approach of incorporating an anatomical prior without lesion outlines to suppress noise while preserving lesions. The convergence could possibly be improved using an auxiliary field and maximizing a joint posterior (Ing-Tsung et al 2003), which is a subject for future work.

Another potential pitfall of AAMDF could be the inhomogeneity of tracer uptake in some organs, which could degrade the accuracy of estimating $K$. To examine the performance of AAMDF in inhomogeneous regions, we simulated this scenario in the physical phantom study by distributing the beads unevenly in the lung regions (figure 3(a)). It can be observed from the reconstruction results (figure 12) that AAMDF alleviated the piecewise smoothness seen in the MRP and AMDF reconstructions. This reveals that the estimation of $K$ is relatively robust to moderate heterogeneity in an organ region. However, a large variation in the image gradient magnitude may cause more degradation in the estimation of $K$. We will investigate the performance of the proposed algorithm with lumpy backgrounds in future work. In addition, the parameter $K$ was empirically set to a relatively small value (70%) of the local standard deviation within each anatomical region in this study. Although this approach demonstrated superior performance than other related methods tested in our experiments, a more theoretically rigorous edge estimator may be preferable.

Finally, the incorporation of the anisotropic diffusion process requires more computation than the conventional MAP with quadratic prior. In this study, all the reconstructions were carried out on a workstation with an Intel Xeon Processor at 2.66 Ghz in the IDL (ITT™) environment. With 40 iterations and 8 subsets, the average reconstruction time for a single slice with AAMDF prior was 12 s, as compared to 3 s for MAP. However, with advances in multi-core and parallel processing computing technology, it may be possible to reduce these times significantly, such that the differences in computational time may become negligible.
Anisotropic diffusion filtering may be seen as a gradient descent of some non-convex energy function (Perona and Malik 1990, Lalush and Tsui 1992). Similar to the ADF, several non-convex priors have been proposed using a parameter for tuning the edge height above which the pixel difference is encouraged to be preserved in MAP reconstruction (Lalush and Tsui 1992, 1993). The applications of those priors in emission tomography have the same difficulty of selecting an accurate edge preserving parameter value to distinguish the gradient magnitude produced by edges from those produced by noise. We expect that our approach of using the anatomical prior for both estimation of the edge preserving parameter and for guiding the PET reconstruction could also be extended to those priors. A comparison of the AAMDF prior with other non-convex priors is an interesting area for further investigation.

In summary, we have performed simulation and physical phantom studies and demonstrated that the proposed AAMDF prior yields improved lesion contrast and reduced bias without requiring knowledge of lesion outlines, especially for lesions that are remote from organ boundaries. Visual assessment of the images also reveals that the proposed method yields accurate organ boundaries, thus aiding lesion localization and markedly reducing the stepwise smoothness seen with the MRP and AMDF priors. These findings suggest some promise for the AAMDF prior in clinical PET/CT, where the utility of anatomical priors is often restricted by the limitations of the CT data, and we will assess the clinical value of this and other approaches involving anatomical priors in future studies.

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