Investigation of statistical iterative reconstruction for dedicated breast CT

Andrey Makeev and Stephen J. Glick^{a)}

UMass Medical School, 55 Lake Avenue North, Worcester, Massachusetts 01655

(Received 17 September 2012; revised 15 April 2013; accepted for publication 22 May 2013; published 3 July 2013)

Purpose: Dedicated breast CT has great potential for improving the detection and diagnosis of breast cancer. Statistical iterative reconstruction (SIR) in dedicated breast CT is a promising alternative to traditional filtered backprojection (FBP). One of the difficulties in using SIR is the presence of free parameters in the algorithm that control the appearance of the resulting image. These parameters require tuning in order to achieve high quality reconstructions. In this study, the authors investigated the penalized maximum likelihood (PML) method with two commonly used types of roughness penalty functions: hyperbolic potential and anisotropic total variation (TV) norm. Reconstructed images were compared with images obtained using standard FBP. Optimal parameters for PML with the hyperbolic prior are reported for the task of detecting microcalcifications embedded in breast tissue.

Methods: Computer simulations were used to acquire projections in a half-cone beam geometry. The modeled setup describes a realistic breast CT benchtop system, with an x-ray spectra produced by a point source and an a-Si, CsI:TI flat-panel detector. A voxelized anthropomorphic breast phantom with 280 μm microcalcification spheres embedded in it was used to model attenuation properties of the uncompressed woman's breast in a pendant position. The reconstruction of 3D images was performed using the separable paraboloidal surrogates algorithm with ordered subsets. Task performance was assessed with the ideal observer detectability index to determine optimal PML parameters.

Results: The authors' findings suggest that there is a preferred range of values of the roughness penalty weight and the edge preservation threshold in the penalized objective function with the hyperbolic potential, which resulted in low noise images with high contrast microcalcifications preserved. In terms of numerical observer detectability index, the PML method with optimal parameters yielded substantially improved performance (by a factor of greater than 10) compared to FBP. The hyperbolic prior was also observed to be superior to the TV norm. A few of the best-performing parameter pairs for the PML method also demonstrated superior performance for various radiation doses. In fact, using PML with certain parameter values results in better images, acquired using 2 mGy dose, than FBP-reconstructed images acquired using 6 mGy dose.

Conclusions: A range of optimal free parameters for the PML algorithm with hyperbolic and TV norm-based potentials is presented for the microcalcification detection task, in dedicated breast CT. The reported values can be used as starting values of the free parameters, when SIR techniques are used for image reconstruction. Significant improvement in image quality can be achieved by using PML with optimal combination of parameters, as compared to FBP. Importantly, these results suggest improved detection of microcalcifications can be obtained by using PML with lower radiation dose to the patient, than using FBP with higher dose. © 2013 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4811328>]

Key words: breast CT, microcalcification detection, iterative reconstruction, penalized maximum likelihood, Huber prior, total variation norm

1. INTRODUCTION

A number of research groups have been investigating the potential of dedicated breast CT for improving the detection and diagnosis of breast cancer. Preliminary clinical studies have suggested that breast CT provides good visualization of both masses and microcalcifications using a radiation dose approximately equivalent to that of mammography. With a few exceptions,¹ most prototype breast CT systems being tested perform reconstruction using Feldkamp's cone-beam filtered backprojection (FBP) algorithm² (nonstatistical).

In the past few years, there has been a renewed interest in the use of iterative reconstruction techniques for CT. The

motivating factors for this focus include the increasing availability of inexpensive computer power, as well as the potential for improved image quality and lower radiation dose. Although a number of studies have investigated the performance of iterative reconstruction for CT,³ very few have been addressed specifically to the upcoming new modality of breast CT. Previously, Das *et al.*⁴ observed improvements in the accuracy of detecting microcalcifications, when using statistical iterative reconstruction (SIR) for breast tomosynthesis. In this study, we investigate SIR algorithms for breast CT. There are a number of possible advantages of using SIR for breast CT. First, SIR algorithms provide a better model of photon statistics in the reconstruction process than standard filtered

backprojection, possibly leading to lower reconstruction noise. This observation is particularly true for CT imaging under conditions of low x-ray fluence. Since breast CT aims to provide similar radiation dose to mammography, the x-ray fluence incident on the detector when imaging medium to large size breasts can be relatively low. Acquiring low-dose breast CT scans is desirable, particularly for screening or contrast-enhanced dynamic CT applications. Another advantage of SIR for cone-beam CT is the possibility of reducing artifacts due to incomplete sampling with circular orbit breast CT.⁵ A third advantage of SIR is the possible reduction of angular aliasing artifacts, especially for acquisitions with lower number of projection views.⁶ Using a large number of projection views in low-dose breast CT can be prohibitive due to the relatively increasing impact of detector electronic noise at low x-ray fluence. A fourth advantage of SIR compared to FBP is that SIR algorithms are more forgiving when projection truncation is present. Thus, SIR algorithms might be beneficial for imaging volumes of interest (VOI) within the breast. Here, we investigate SIR using the penalized likelihood objective function with two commonly used roughness penalty terms, the hyperbolic potential and anisotropic total variation norm.

To evaluate reconstructions obtained with these algorithms and to compare performance to standard filtered-backprojection, a computer simulation study was performed using microcalcifications embedded into an anthropomorphic breast phantom. Visualizing microcalcifications in x-ray breast imaging systems is important for the detection of ductal carcinoma *in situ* (DCIS). It has been estimated that DCIS represents 20%–30% of all breast cancer detected in a screening program.⁷ Since at least 30%–50% of all DCIS eventually become invasive if not treated, early detection and diagnosis of DCIS contributes to a decreased breast cancer mortality rate. With conventional mammography, Feig *et al.*⁸ and Anderson⁹ reported that 89% and 95%, respectively, of DCIS were observed on the basis of microcalcifications alone. Thus, to compete with conventional mammography, it is important that radiologists are able to accurately detect and diagnose microcalcifications on breast CT imaging devices.⁸

Section 2.A gives a brief review of the algorithms used to obtain image reconstructions that maximize the penalized likelihood objective function and in Secs. 2.C and 2.D, we describe a computer simulation study to generate realistic breast CT projections. Section 2.E describes the ideal observer model that is used as a figure-of-merit. Section 3 presents results demonstrating the improved performance of the penalized maximum likelihood (PML) algorithm, and Sec. 4 provides some conclusions of this study.

2. METHODS

2.A. Reconstruction algorithm

In dedicated breast CT projection images are commonly acquired in a truncated cone-beam geometry over a complete circular orbit. Statistical iterative reconstruction of projections is performed by maximizing the objective function

$$\Phi(\boldsymbol{\mu}) = L(\boldsymbol{\mu}) - \beta R(\boldsymbol{\mu}), \quad (1)$$

where L is the log-likelihood, R is the roughness penalty, β is the penalty weight, $\boldsymbol{\mu}$ is a vector of the voxel attenuation values. The logarithm of the likelihood function for the transmission measurements with N detector pixels and p voxels in the attenuation map^{10,11}

$$L(\boldsymbol{\mu}) = \sum_{i=1}^N [y_i \ln(b_i e^{-l_i}) - b_i e^{-l_i}], \quad (2)$$

is obtained using the statistical model $y_i \sim \text{Poisson}\{b_i e^{-l_i}\}$ for the number of photons registered by the i th detector pixel. Here, b_i is the blank scan photon count, and the line integral over the i th ray is given by $l_i = \sum_{j=1}^p a_{ij} \mu_j$, where a_{ij} are the elements of the $N \times p$ system matrix. The roughness penalty term can be expressed in the form¹¹

$$R(\boldsymbol{\mu}) = \frac{1}{2} \sum_{j=1}^p \sum_{k \in N_j} \omega_{jk} \psi(\mu_j - \mu_k), \quad (3)$$

where the inner summation is over j th voxel's neighbors, the outer summation is over all the voxels in the object, ψ is the potential function, that determines how the differences between neighboring voxel attenuation values contribute to the penalty, and the weight factors $\omega_{jk} = \omega_{kj}$ are the reciprocates of the distances between voxels centers. The objective function (1) was maximized using the separable paraboloidal surrogates algorithm with ordered subsets (SPS OS) developed by Erdogan and Fessler.¹⁰ It combines the optimization transfer principle to maximize the global surrogate $\phi(\boldsymbol{\mu}; \boldsymbol{\mu}^n) = Q_2(\boldsymbol{\mu}; \boldsymbol{\mu}^n) + \beta S(\boldsymbol{\mu}; \boldsymbol{\mu}^n)$ for the original objective function $\Phi(\boldsymbol{\mu})$ and Newton's method to solve the optimization problem iteratively

$$\mu_j^{(n+1)} = \mu_j^{(n)} + \frac{\dot{L}_j - \beta \sum_k \omega_{jk} \dot{\psi}(\mu_j^{(n)} - \mu_k^{(n)})}{d_j^* + 2\beta \sum_k \omega_{jk} \omega_{\psi}(\mu_j^{(n)} - \mu_k^{(n)})}, \quad (4)$$

where $\omega_{\psi}(x) = \dot{\psi}(x)/x$, and the terms $d_j^* = \sum_{i=1}^N (y_i a_{ij} \sum_{j=1}^p a_{ij})$ are precomputed before iterating.

2.B. Edge-preserving potential functions

We investigated two commonly used types of potential functions which retain high-contrast details: the (Huber-like) hyperbolic function and the anisotropic total variation norm. The hyperbolic function (Fig. 1, left graph) is given by

$$\psi_{\text{hy}}(x) = \delta^2 \left[\sqrt{1 + \left(\frac{x}{\delta}\right)^2} - 1 \right], \quad (5)$$

where $x = \mu_j - \mu_k$ is the difference between neighboring voxel values, and the parameter δ determines the edge-preservation threshold. Equation (5) is, in fact, an asymptotic approximation of the Huber function, an often used edge-conserving potential. Notice that the hyperbolic potential is quadratic $\psi_{\text{hy}}(x) \approx x^2/2$, for $|x| \ll \delta$, but becomes linear $\psi_{\text{hy}}(x) \approx \delta^2(|x|/\delta - 1)$, for $|x| \gg \delta$. Therefore, smoothing over low-contrast areas $|x| \ll \delta$ is applied linearly $\dot{\psi}_{\text{hy}}(x) \approx x$, while for high-gradient edges $|x| \gg \delta$, $\dot{\psi}_{\text{hy}}(x) \approx \delta x/|x|$, i.e., smoothing is *constant* (Fig. 1, right graph), such that the relative penalty becomes smaller

FIG. 1. Hyperbolic function $\psi_{hy}(x)$ (left panel) and its derivative $\psi'_{hy}(x)$ (right panel). Dashed lines indicate edge-preserving threshold δ .

with increasing x . Clearly, the choice of the free parameters β and δ in the penalized likelihood objective function (1) can significantly affect the appearance of the reconstruction. A similar type of edge-conserving potential function is based on the definition of the total variation norm. Over the vicinity of a given voxel in 3D the anisotropic TV norm is given by

$$\begin{aligned} \psi_{TV}(\mu_{i,j,k}) = & |\mu_{i,j,k} - \mu_{i-1,j,k}| + |\mu_{i,j,k} - \mu_{i+1,j,k}| \\ & + |\mu_{i,j,k} - \mu_{i,j-1,k}| + |\mu_{i,j,k} - \mu_{i,j+1,k}| \\ & + |\mu_{i,j,k} - \mu_{i,j,k-1}| + |\mu_{i,j,k} - \mu_{i,j,k+1}|. \end{aligned} \quad (6)$$

As defined, this function suffers the derivative discontinuity at $x = 0$. In order to maintain the objective function differentiable in the immediate proximity of $x = 0$, each (n th) constituent of the sum in Eq. (6) can be modified by introducing an arbitrary small positive constant ϵ , such that

$$\psi_{TV}^{(n)}(x) = \begin{cases} |x| & \text{for } |x| > \epsilon, \\ x^2/2\epsilon + \epsilon/2 & \text{for } |x| \leq \epsilon. \end{cases} \quad (7)$$

Modified in this way, components of the TV norm penalty ensure both the function's and its derivative's continuity at the origin, at points $x = \pm\epsilon$, as well as make $\psi_{TV}^{(n)}(x) = 0$ if x is exactly zero. It should be mentioned that the TV function (7) uses six neighbors to evaluate the voxel value difference, compared to 26 neighbors used in the hyperbolic function (5).

2.C. Breast CT simulation setup

Simulated projections were acquired using the UMass cone-beam simulation software,¹² which models the operation of a breast CT system in a truncated cone-beam geometry (Fig. 2). The model setup consists of a point x-ray source, an indirect-conversion a-Si, CsI:TI flat-panel detector array, and an object positioned between the source and the detector. In the software, the detector and the source can be rotated simultaneously by the same angle. For this study, we modeled a 50 kVp tungsten anode photon spectrum,¹³ filtered with 0.9 mm aluminum, attenuated by an anthropomorphic digi-

tal breast phantom, and detected by a Varian PaxScan 2520 imager with 2×2 binning. This produced 960×768 pixel projections of the phantom with a $254 \mu\text{m}$ pixel pitch. Complete signal and noise transport, including conversion gains,¹⁴ photon Poisson noise, electronic noise, optical spreading in a 0.6 mm scintillator, as well as x-ray tube focal spot blurring, was modeled. X-ray scatter was not modeled in the study. The Siddon ray tracing algorithm¹⁵ was used for x-ray transport through the breast phantom. 360 projections were acquired over a complete circular orbit, to be reconstructed with the Feldkamp, David, and Kress filtered backprojection cone-beam algorithm² and the iterative PML reconstruction method, using the two priors previously discussed. For the PML parameter sweep study, we used a total dose of 3 mGy which corresponds to a typical exposure in a clinical two-view mammography, while for the algorithm's performance comparison at different dose settings it was varied between 0.5 and 6 mGy. This was accomplished by scaling the x-ray fluence, using precomputed normalized glandular dose coefficients.¹⁶

2.D. Digital breast phantom with microcalcifications

A $600 \times 600 \times 250 \text{ vx}^3$ anthropomorphic breast phantom (Fig. 3), with a $200 \mu\text{m}$ cubical voxel, was selected from an ensemble of phantoms generated from CT acquisitions of surgical mastectomy specimens.¹⁷ The numerical phantom models an uncompressed breast in the pendant position, which is a proposed setup for dedicated breast CT. Microcalcifications

FIG. 2. Schematic representation of a dedicated breast CT apparatus.

FIG. 3. Voxelized breast phantom BU53L used for reconstruction.

in the breast tissue were simulated as $280\ \mu\text{m}$ spheres with x-ray absorption properties of hydroxyapatite, randomly embedded in $N = 100$ consecutive axial slices of the phantom, with one sphere in each slice. Ray tracing through the breast background was performed with $200\ \mu\text{m}$ cubic voxels, whereas ray tracing through microcalcifications used fine $20\ \mu\text{m}$ cubic voxels.

2.E. Numerical model observer as a figure of merit

To objectively assess performance of the reconstruction algorithms in the detection task, a numerical model observer was used. Similar to the ideal observer detectability index d_{ideal}^2 for a SKE task with stationary noise and background,¹⁸ we used the detectability index defined¹⁹ as

$$d^2 = \sum_{\mathbf{k}} \frac{|S(\mathbf{k})|^2}{P(\mathbf{k})}, \quad (8)$$

where $S(\mathbf{k})$ is the discrete Fourier transform (DFT) of the deterministic signal, $P(\mathbf{k})$ is the background noise power spectrum, and $\mathbf{k}$ is the radial frequency vector. Two reconstructions of the breast phantom were produced to simulate signal present, signal absent ROIs: one, with microcalcification spheres inserted and Poisson/electronic noise present, and a noise-free reconstruction of the phantom background.^{18–20} The signal mask was defined in a 128×128 vx² region of a transaxial phantom slice, with the microcalcification positioned in the center. Then, the difference between the signal present $\mathbf{g}^{\text{sig}}$ and noise-free background $\mathbf{g}^{\text{nf bkg}}$ images, averaged over the number of samples, was used to compute a 2D signal spectrum

$$S(\mathbf{u}, \mathbf{v}) = \mathcal{F} \left\{ \mathbf{W}_H \left[\frac{1}{N} \sum_{i=1}^N (\mathbf{g}_i^{\text{sig}} - \mathbf{g}_i^{\text{nf bkg}}) \right] \right\}, \quad (9)$$

with a radially symmetric Hann window

$$\mathbf{W}_H = \begin{cases} 1/2[1 + \cos(\pi r/R)] & \text{for } r \leq R, \\ 0 & \text{for } r > R, \end{cases} \quad (10)$$

applied to the image, prior to computing a DFT, in order to minimize spectral leakage. In formula (10), $r = \sqrt{(x - x_0)^2 + (y - y_0)^2}$ is the distance from the ROI center to a voxel at (x, y) , $R = 64$.

Likewise, a 2D noise power spectrum was computed as the ensemble-average spectrum over N ROIs, randomly sampled in the different slices of the phantom

$$P(\mathbf{u}, \mathbf{v}) = \frac{1}{N} \sum_{j=1}^N |\mathcal{F} \{ \mathbf{W}_H (\mathbf{g}_j - \mathbf{g}_j^{\text{nf}}) \}|^2. \quad (11)$$

Finally, to further reduce noise in the stochastic noise power spectrum, the two-dimensional DFTs (9) and (11) were radially averaged to 1D to calculate d^2 .

2.F. Implementation of reconstruction methods

To ensure a fair comparison between the two types of algorithms, the effect of a smoothing filter on microcalcification detectability in the FBP images was investigated. Filtering out high-frequency components in the image reduces noise in the areas of the homogeneous background, but also smears fine details at the high-contrast tissue boundaries. Postreconstruction processing was done using the Butterworth low-pass filter $B(f) = 1/[1 + (f/f_0)^{2n}]$ with various values of the cut-off frequency ($0.05 \leq f_0 \leq 0.4\ \text{px}^{-1}$) and the order of the filter $n = 5$. The filtered FBP images were compared with each other based on the detectability for a specific detection task. For this testing, we used a set of 360 projections of a $120 \times 120 \times 50\ \text{mm}^3$ breast phantom, populated with $280\ \mu\text{m}$ diameter microcalcifications, acquired with a 3 mGy dose. Our results showed that higher values of the cut-off frequency f_0 in the filter consistently produced increasingly better values of the detectability index. Consequently, FBP reconstruction with the unwrapped ramp filter had the highest detectability value $d_{\text{FBP}}^2 = 7.1 \pm 0.3$, and, hence, was chosen to perform a comparison with the iterative algorithm.²¹

In the PML method, we used 25 iterations with 30 ordered subsets for both penalty functions and all parameter combinations. The number of ordered subsets was selected based on practical considerations of running 12 projection tasks for a given subset, simultaneously, on a 12-core CPU, for 360 projections. The selection of an appropriate stopping iteration is challenging for comparisons of iterative algorithms. Figure 4 shows how the numerical observer detectability index changes with the iteration number for the PML method for a few parameter combinations in the hyperbolic and TV norm potential functions. Although, the values of d^2 do not stabilize for either prior for the highest iteration shown, the trends are clear: the TV prior detectability varies rather slowly compared to the hyperbolic one, neither does it achieve the performance of the hyperbolic prior. Our existing implementation of the SPS OS algorithm is not parallelized to do concurrent update of the reconstructed voxels and needs ≈ 0.5 h/iteration for the given projection and phantom dimensions. Therefore, the computational load required for the iterative method was a major deciding factor in choosing the stopping iteration. In this work, we did not address the problem of how the change in the algorithm parameters affects its convergence properties, but rather state subjectively that after a certain number of iterations the method visually provides

FIG. 4. Detectability index as a function of iteration number for the SPS OS algorithm with hyperbolic and TV norm priors.

high-quality images for both potential functions under investigation.

The 200 μm reconstruction voxel size was used to emulate a typical clinical breast CT setup, in which the projection pixel and the reconstruction voxel sizes are related via geometric magnification $1\text{px} \sim M\text{lvx}$. In this case, a 280 μm diameter microcalcification may occupy only two voxels in each dimension.

3. RESULTS AND DISCUSSION

3.A. PML method with the hyperbolic prior

A sweep over a total of 192 parameter combinations was performed, by calculating the detectability index d^2 , to test 12 values of β and 16 values of δ in the penalized objective function with the hyperbolic potential

$$\Phi(\mu) = L(\mu) - \frac{\beta\delta^2}{2} \sum_{j=1}^p \sum_{k \in N_j} \omega_{jk} \left[\sqrt{1 + \left(\frac{\mu_j - \mu_k}{\delta} \right)^2} - 1 \right]. \quad (12)$$

The smoothness weight in Eq. (12) was varied within the $5 \times 10^5 \leq \beta \leq 5 \times 10^{10}$ range, and the edge threshold parameter was varied in the $10^{-6} \leq \delta \leq 7.5 \times 10^{-3}$ range, respectively. A subjective visual inspection of the reconstructions showed that the images produced with parameter $\beta < 5 \times 10^7$ came out unacceptably noisy. On the other hand, images reconstructed with $\beta > 10^9$ appear to have unnatural, patchy background texture. Both these ranges resulted in reconstructions with relatively low values of the detectability index, and therefore were discarded from further analysis. The results for the remaining 96 $\beta - \delta$ combinations are summarized in Fig. 5. The model observer detectability index d^2 is plotted as a function of the edge-preserving parameter δ (log scale is used on x axis), where different symbols represent corresponding values of the penalty weight β . Each point on the graph is computed as the average of ten

FIG. 5. Detectability index for various combinations of parameters β and δ in the SPS OS algorithm with the hyperbolic potential function. Smooth lines connecting the points for the three best parameter combinations added for clarity.

simulated measurements with the uncertainty $\Delta d^2 = (d_{\max}^2 - d_{\min}^2)/2$. Performance of the FBP algorithm is indicated by a dashed line. About 80% of all points on the graph fall in the range of the detectability index close to that of FBP ($d_{\text{FBP}}^2 = 7.1 \pm 0.3$), with the exception of a few notable combinations, concentrated in the region $2 \times 10^{-5} < \delta < 2 \times 10^{-4}$, which produced substantially higher values of d^2 . The best pair $\beta = 5 \times 10^8$, $\delta = 7.5 \times 10^{-5}$ resulted in an image with $d_{\text{PML,hy}}^2 = 91 \pm 5$, which exceeds that for the FBP by more than a factor of 10. Based on these results, we estimate that the optimal range of the PML free parameters, using the hyperbolic potential function, for microcalcification detection in a breast tissue is contained in a range

$$5 \times 10^8 \leq \beta \leq 10^9, \\ 5 \times 10^{-5} \leq \delta \leq 10^{-4}.$$

It is important to notice that the high detectability values reported here for optimized PML parameter combinations should not exaggerate their clinical significance. Under the assumption of Gaussian noise, the detectability index can be converted to the receiver operating characteristic (ROC) area under the curve (AUC) as

$$\text{AUC} = \frac{1}{2} \text{erf} \left(\frac{d'}{2} \right) + \frac{1}{2}. \quad (13)$$

Using this expression can provide some insight into the difficulty of the task studied. For example, for the reference FBP reconstruction $\text{AUC}_{\text{FBP}} = 0.97$, whereas using the optimal PML parameters, $\text{AUC}_{\text{PML}} \approx 1$. This suggests that the task of detecting a 280 μm microcalcification with 3 mGy dose is somewhat easy, nonetheless reconstruction with PML does provide a small improvement. As discussed below, PML provides a more substantial improvement in the AUC for the low-dose case.

FIG. 6. Detectability index as a function of penalty weight β in the SPS OS algorithm with the TV norm prior.

3.B. PML method with the TV norm prior

The same figure of merit for the task-based evaluation of image quality was used to test the PML method with the anisotropic total variation penalty. For the TV prior, it is only a single parameter β in Eq. (4) that controls appearance of the output image. We analyzed 24 reconstructions with varying smoothness strength β that covered a range $7 \times 10^3 \leq \beta \leq 1.5 \times 10^5$. This is demonstrated in Fig. 6. There is a preferred region of the parameter values, centered around $\beta = 6.5 \times 10^4$, where the detectability index reaches its maximum value of $d_{\text{PML,TV}}^2 = 22.1 \pm 0.3$. This is three times better performance than that achieved with the FBP algorithm, but inferior to the detectability obtained with the PML algorithm using the hyperbolic potential and optimal $\beta - \delta$ combination. Such a result was somewhat anticipated, since, first, the TV norm-based prior is essentially equivalent to the hyperbolic function with $\delta \rightarrow 0$, second, the anisotropic TV function uses only six neighbors of a given voxel, in three dimensions, to compute the penalty term, whereas the hyperbolic prior uses all 26 neighbors, providing complete representation of the clique. Apparently, the two parameters in the

hyperbolic prior allow for more flexibility in adjusting image quality.

3.C. Image comparison for the three methods

Shown in Fig. 7 are nine 128×128 vx² ROIs from the reconstructed slices of the breast phantom with the microcalcification located in the center (please view electronic version of paper for best display). Images for each method are combined in a square grid, with filtered backprojection images displayed on the left, followed by the PML reconstruction using the TV penalty with $\beta = 6.5 \times 10^4$, and the PML reconstruction using the hyperbolic potential with $\beta = 5 \times 10^8$, $\delta = 7.5 \times 10^{-5}$ shown on the right. As can be observed, the PML algorithm with optimal parameters for both priors studied yielded significantly less noisy images than FBP, maintaining at the same time, microcalcification sharpness.

3.D. Varying radiation dose: PML vs FBP

Better modeling of photon statistics provides advantages to the iterative reconstruction methods as compared to standard FBP, especially in low x-ray fluence scans. We compared the performance of the PML algorithm with the hyperbolic prior and four best $\beta - \delta$ combinations, TV prior with optimal penalty weight β , and FBP, for several values of mean glandular dose, varying from 0.5 to 6 mGy. These results are summarized in Fig. 8. The main interest in the SIR method is in the low dose imaging region. At 2 mGy the iterative algorithm with hyperbolic and TV priors shows noticeable advantage over FBP. Particularly, PML with $\beta = 5 \times 10^8$, $\delta = 5 \times 10^{-5}$ results in $d^2 = 47$ (AUC ≈ 1), while FBP at this dose produces an image with $d^2 = 4.4$ (AUC = 0.93). This difference becomes more significant for 1 mGy dose, for which the best-performing PML parameter pair $\beta = 2.5 \times 10^8$, $\delta = 7.5 \times 10^{-5}$ has $d^2 = 11.9$ (AUC = 0.99) compared to $d^2 = 1.59$ (AUC = 0.81) for FBP. For the smallest dose of 0.5 mGy PML with $\beta = 2.5 \times 10^8$, $\delta = 7.5 \times 10^{-5}$ produces $d^2 = 1.26$ (AUC = 0.79), with FBP resulting in $d^2 = 0.725$ (AUC = 0.73), while all other PML parameter

FIG. 7. Example of nine reconstructed signal ROIs arranged in 3×3 array. From left to right are images obtained using: FBP with no filtering, PML/TV norm prior with $\beta = 6.5 \times 10^4$, PML/hyperbolic prior with $\beta = 5 \times 10^8$, $\delta = 7.5 \times 10^{-5}$. Attenuation coefficient values were scaled into the range 0–255; window center $w_c = 128$ and window width $w_w = 256$ were used for display scale throughout.

FIG. 8. Index d^2 as a function of dose for the PML algorithm with the hyperbolic prior (few parameter combinations), TV norm prior with optimal β , and FBP. Smooth lines added to emphasize the trends.

combinations gave slightly lower d^2 . For the dose settings from 3 to 6 mGy, the PML method performs substantially better than the FBP. It is noteworthy to observe that all four PML sets of parameters result in a higher value of index d^2 at 2 mGy dose than FBP at 6 mGy. Although, the TV norm potentially outperformed FBP for all studied doses but 0.5 mGy, it shows noticeably weaker detectability when compared to the optimally tuned hyperbolic prior. Obviously, there is a potential to improve image quality in low fluence breast CT scans by using iterative algorithms with optimized free parameters. However, it seems that no “universal” best PML parameter combination exists for all range of exposures, but rather the algorithm should be specifically tuned for each dose individually.

4. CONCLUSIONS

In this study, we examined the use of iterative reconstruction using a PML objective function with two different commonly used penalty functions, namely, the hyperbolic function prior and the anisotropic TV norm. Realistic computer simulations of breast CT were conducted by embedding small microcalcification spheres into an anthropomorphic breast phantom background. An ideal observer model, otherwise referred to as the detectability index d^2 , was used to objectively assess performance of the different algorithms. A few important conclusions can be made from the results.

First, the selection of free-parameters in the penalty function had a large impact on detectability. Using the hyperbolic prior, it was observed that most parameter choices provided very little benefit over FBP, however, there was a small subset of the parameter space that produced substantially higher d^2 values. It was observed that the TV norm prior also had a small subset of parameter space that provided improvements over FBP, however, the improvement in d^2 was not as great as with the hyperbolic prior. This result was not surprising because it can be shown that the TV norm-based prior is essentially equivalent to the hyperbolic prior as parameter δ ap-

proaches zero. In general, these results emphasize the need for optimizing iterative reconstruction algorithms to maximize performance of a specified diagnostic task.

Second, the results suggested that PML reconstruction provided improved performance over FBP, even with a substantial reduction in radiation dose. There has been a renewed effort of late to reduce dose in CT,²⁰ and it appears as if iterative reconstruction algorithms can contribute to this effort. This finding could be especially important if breast CT were ever to be used for screening asymptomatic women, where annual or biannual scans would be required.

Although the results presented here highly suggest that the accuracy of microcalcification detection can be improved with iterative reconstruction, there are a number of limitations with this study, and thus the results must be interpreted with some caution. The defined task in this study was the detection of a single spherical microcalcification of size 280 μm . This size was selected to provide a challenging detection task. However, microcalcifications typically present in clusters, are not necessarily spherical, and range in size from sub-100 μm to a few mm. The use of a more realistic microcalcification cluster model will be the subject of future work. One promising model was recently developed by Shaheen *et al.*²¹ and is based on micro-CT scans of biopsy specimens containing microcalcification clusters. Another possible limitation concerns the realism of the simulation model. Although many physical factors that model signal and noise transport through the detector are included in the simulation, others such as the non-stationary, anisotropic blurring caused by x rays entering into the detector at oblique angles are not modeled. Freed *et al.*²² have recently proposed an angle dependent model of the CsI response that could, in principle, be included into the likelihood function expressed in Eq. (2).

A variety of figures-of-merit have been used to evaluate image quality and compare iterative reconstruction methods to standard FBP, including, spatial resolution defined through various small structures, modulation transfer function, noise power spectra, contrast-to-noise ratio, signal-to-noise ratio, and subjective visual impression. The figure-of-merit used here is an objective model observer that is designed to assess performance for a specified diagnostic task (e.g., detection of microcalcifications). Ultimately, the real test of whether PML can improve performance in detecting and diagnosing microcalcifications should be achieved using psychophysical observer studies with clinical data read in a clinical environment by radiologist observers.

ACKNOWLEDGMENTS

The authors would like to acknowledge Bing Feng and Mini Das for their help in the implementation of the PML algorithm. This study was supported in part by the National Institutes of Health (NIH) under Grant Nos. RO1 CA140400 and R21 CA134128 from the National Cancer Institute (NCI). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH or NCI.

^{a)}Electronic mail: Stephen.Glick@umassmed.edu

- ¹R. L. McKinley, M. P. Tornai, E. Samei, and M. L. Bradshaw, "Initial study of quasi-monochromatic x-ray beam performance for x-ray computed mammotomography," *IEEE Trans. Nucl. Sci.* **52**, 1243–1250 (2005).
- ²L. A. Feldkamp, L. C. Davis, and J. W. Kress, "Practical cone-beam algorithm," *J. Opt. Soc. Am.* **1**, 612–619 (1984).
- ³M. Beister, D. Kolditz, and W. A. Kalender, "Iterative reconstruction methods in X-ray CT," *Physica Medica* **28**(2), 94–108 (2012).
- ⁴M. Das, H. C. Gifford, J. M. O'Connor, and S. J. Glick, "Penalized maximum likelihood reconstruction for improved microcalcification detection in breast tomosynthesis," *IEEE Trans. Med. Imaging* **30**(4), 904–914 (2011).
- ⁵S. Vedantham, L. Shi, F. Noo, S. J. Glick, and A. Karellas, "Cone-beam artifacts in dedicated breast CT," SU-E-I-150, Annual AAPM Meeting, Vancouver, Canada, 2011.
- ⁶X. Han, J. Bian, E. L. Ritman, E. Y. Sidky, and X. Pan, "Optimization-based reconstruction of sparse images from few-view projections," *Phys. Med. Biol.* **57**, 5245–5273 (2012).
- ⁷D. B. Kopans, *Breast Imaging* (Lippincott-Raven, Philadelphia, 1998).
- ⁸S. A. Feig, G. S. Shaber, A. Patchefsky, G. F. Schwartz, J. Edeiken, H. I. Libshitz, R. Nerlinger, R. F. Curley, and J. D. Wallace, "Analysis of clinically occult and mammographically occult breast tumors," *AJR, Am. J. Roentgenol* **128**(3), 403–408 (1977).
- ⁹I. Anderson, "Mammographic screening for breast carcinoma," Ph.D. thesis, Lund University, Malmö, Sweden, 1980.
- ¹⁰H. Erdogan and J. A. Fessler, "Ordered subsets algorithms for transmission tomography," *Phys. Med. Biol.* **44**, 2835–2851 (1999).
- ¹¹J. A. Fessler, "Statistical image reconstruction methods for transmission tomography," *SPIE Handbook of Medical Imaging* (SPIE, International Society for Optical Engineering, Bellingham, WA, 2000), Vol. 2.
- ¹²A. A. Vedula, S. J. Glick, and X. Gong, "Computer simulation of CT mammography using a flat-panel imager," *Proc. SPIE* **5030**, 349–360 (2003).
- ¹³J. M. Boone and J. A. Seibert, "An accurate method for computer-generating tungsten anode x-ray spectra from 30 to 140 keV," *Med. Phys.* **24**(11), 1661–1670 (1997).
- ¹⁴D. J. Tward and J. H. Siewerdsen, "Cascaded systems analysis of the 3D noise transfer characteristics of flat-panel cone-beam CT," *Med. Phys.* **35**(12), 5510–5529 (2008).
- ¹⁵R. L. Siddon, "Fast calculation of the exact radiological path for a three-dimensional CT array," *Med. Phys.* **12**(2), 252 (1985).
- ¹⁶S. C. Thacker and S. J. Glick, "Normalized glandular dose (DgN) coefficients for flat-panel CT breast imaging," *Phys. Med. Biol.* **49**, 5433–5444 (2004).
- ¹⁷J. M. O'Connor, M. Das, C. Didier, M. Mah'd, and S. J. Glick, "Development of an ensemble of digital breast object models," *Proceedings of International Workshop on Digital Mammography*, Lecture Notes in Computer Science, Girona, Catalonia, Spain, Vol. 6136, 54–61, 2010.
- ¹⁸A. E. Burgess, F. L. Jacobson, and P. F. Judy, "Human observer detection experiments with mammograms and power-law noise," *Med. Phys.* **28**(4), 419–437 (2001).
- ¹⁹J. Bian, J. H. Siewerdsen, X. Han, E. Y. Sidky, J. L. Prince, C. A. Pelizzari, and X. Pan, "Evaluation of sparse-view reconstruction from flat-panel-detector cone-beam CT," *Phys. Med. Biol.* **55**, 6575–6599 (2010).
- ²⁰C. H. McCollough, A. N. Primak, N. Braun, J. Kofler, L. Yu, and J. Christner, "Strategies for reducing radiation dose in CT," *Radiol. Clin. North Amer.* **47**(1), 27–40 (2009).
- ²¹E. Shaheen, C. Van Ongeval, F. Zanca, L. Cockmartin, N. Marshall, J. Jacobs, K. C. Young, D. R. Dance, and H. Bosmans, "The simulation of 3D microcalcification clusters in 2D digital mammography and breast tomosynthesis," *Med. Phys.* **38**(12), 6659–6672 (2011).
- ²²M. Freed, S. Park, and A. Badano, "A fast, angle-dependent, analytical model of CsI detector response for optimization of 3D X-ray breast imaging systems," *Med. Phys.* **37**(6), 2593–2606 (2010).