Published in final edited form as:

Phys Med. 2017 June ; 38: 23–35. doi:10.1016/j.ejmp.2017.05.001.

Preconditioned alternating projection algorithm for solving the penalized-likelihood SPECT reconstruction problem

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Abstract

Purpose—The authors recently developed a preconditioned alternating projection algorithm (PAPA) for solving the penalized-likelihood SPECT reconstruction problem. The proposed algorithm can solve a wide variety of non-differentiable optimization models. This work is dedicated to comparing the performance of PAPA with total variation (TV) regularization (TV-PAPA) and a novel forward-backward algorithm with nested expectation maximization (EM)-TV iteration scheme (FB-EM-TV).

Methods—Monte Carlo technique was used to simulate multiple noise realizations of the fan-beam collimated SPECT data for a piecewise constant phantom with warm background, and hot and cold spheres with uniform activities at two noise levels. They were reconstructed using the aforementioned algorithms with attenuation, scatter, distance-dependent collimator blurring and sensitivity corrections. Noise suppressing performance, lesion detectability, lesion contrast, contrast recovery coefficient, convergence speed and selection of optimal parameters were evaluated. The conventional EM algorithms with TV post-filter (TVPF-EM) and Gaussian post-filter (GPF-EM) were used as benchmarks.

Results—The TV-PAPA and FB-EM-TV demonstrated similar performance in all investigated categories. Both algorithms outperformed TVPF-EM in terms of image noise suppression, lesion detectability, lesion contrast and convergence speed. We established that the optimal parameters

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Appendix A. Supplementary data: Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ejmp.2017.05.001>.

versus information density approximately followed power laws, which offers a guidance in parameter selection for reconstruction methods.

Conclusions—For the simulated SPECT data, TV-PAPA and FB-EM-TV produced qualitatively and quantitatively similar images. They performed better than the benchmark TVPF-EM and GPF-EM, with only limited loss of lesion contrast.

Keywords

Penalized likelihood SPECT reconstruction; Piecewise constant phantom; Total variation regularization; Fixed-point proximity algorithms

1. Introduction

Single-photon emission computed tomography (SPECT) has contributed enormous benefits to human health over the past decades. However, it involves a fundamental trade-off between image quality and radiation dose to the patient. Increased radiation exposure carries probability of health detriment to the patients, especially the increased risk of getting cancer later in life [1]. Hence, there is a real need to reduce the radiation dose in medical imaging including SPECT studies. Assuming that the imaging time and gamma camera remain unchanged, lower radiation dose can be only achieved by lowering the activity of administered radiotracer. It will inevitably lead to fewer gamma photons in the raw data and thus to increased image noise in the reconstructed images. Such noisy reconstructions might not be clinically useful. Therefore, the challenge is how to reduce the radiation dose in SPECT examinations without compromising the image quality. This can be accomplished by application of better radiotracer, improved imaging hardware, and/or superior reconstruction method. In the present work, we focus on image quality improvement in the lower-dose SPECT studies by implementation of two novel reconstruction methods.

The most commonly used probability distribution for a description of SPECT projection data is the Poisson model [2]. Finding proper estimation of radioactivity distribution based on such a model is a long-standing research problem. Many reconstruction methods for SPECT imaging offer a mechanism for incorporating the Poisson model, and strive to optimize some objective function. For example, the maximum-likelihood (ML) criterion is based on minimizing the negative log-likelihood of projection data conditional on radioactivity distribution. While under the Bayesian framework, the penalized ML estimator seeks a minimizer of the sum of the above negative log-likelihood and a regularization function, which penalizes solutions that have undesirable properties [3]. Different types of regularization functions have been proposed to address issues with various considerations, such as suppression of image noise and artifacts, preservation of image spatial resolution, and enhancement of lesion contrast. Among them we are particularly interested in the total variation (TV) penalty function, which was first proposed by Rudin, Osher and Fatemi [4] and introduced to the field of ECT reconstruction by Jonsson et al. [5] and Panin et al. [6]. The major advantages of TV lie in its preservation of high frequency components of the reconstructed radiopharmaceutical distribution, including discontinuous jumps and steep transitions, and in efficient suppression of image noise.

Many efficient algorithms for TV-regularized optimization models were proposed, including expectation-maximization (EM)-based methods [5–8], projected quasi-Newton methods [9], primal-dual approaches [10], and fixed-point proximity algorithms [11–13]. In particular, a forward-backward splitting algorithm with nested EM-TV iteration scheme (FB-EM-TV) was recently developed in [7] for reconstruction of PET data with a low signal-to-noise ratio, and further justified and analyzed in [8]. The FB-EM-TV was derived using the Karush-Kuhn-Tucker conditions, which formally provided the existence of a Lagrange multiplier such that the stationary points of the underlying model satisfied a certain coupled equation. A semi-implicit approach was developed to search for the desired stationary points, leading to a nested two-step iteration scheme.

On the other hand, our methodology was motivated in a different way [11]. Indeed, by identifying the TV as a composition of the convex function, which defines the ℓ^1 -norm, and the first-order difference operator, we formulated a characterization of the exact solutions to the underlying optimization problem in terms of a system of fixed-point equations via two proximity operators raised from the convex functions that define the TV and the constraint involved in the problem. The proximity operators of these simple functions have closed forms, which provide great computational advantages. The resulting fixed-point characterization naturally led to an alternating projection algorithm. The dense system matrix of large size was treated by preconditioning. Appropriate choices of the preconditioning matrices led to efficient algorithms (preconditioned alternating projection algorithm, PAPA) for finding the solutions.

In this study, we compared the performance of PAPA with TV regularization (TV-PAPA) and the FB-EM-TV on reconstructing fan-beam SPECT data of piecewise constant phantoms with and without simulated hot and cold lesions. Such simple phantoms facilitate direct comparative studies, and the TV regularization is best suited for their reconstruction. In addition, the conventional maximum-likelihood expectation maximization algorithm [14,15] with Gaussian post-filter (GPF-EM) [16] was introduced as a benchmark.

2. Methods

2.1. Penalized maximum likelihood estimation for SPECT reconstruction

It is well established that in SPECT system, the gamma photon emission rate from an ensemble of radionuclei, and subsequent photon detection at a detector element follow the temporal Poisson distribution. Therefore, the projection data $g \in \mathbb{R}^m$ at m detector elements, which relates to the unobservable expected radiotracer activity distribution $f \in \mathbb{R}^d$ in d voxels of the reconstruction volume, can be approximated by the Poisson model [14,15]:

$$g = \text{Poisson}(Af + \gamma). \quad (1)$$

In Eq. (1), A is the $m \times d$ SPECT system matrix with its (i, j) th entry equal to the probability of detection of the photon emitted from voxel j of image f by the i th detector element, and γ

$\in \mathbb{R}^m$ is the vector containing expected background counts due to the out of field activity and scattered activity.

Given a realization of g , our goal is to reconstruct f while suppressing Poisson noise and preserving spatial resolution in the estimate. We formulate the reconstruction problem via the penalized maximum likelihood (ML) criterion. In fact, the penalized ML estimate is obtained by maximizing the sum of log-likelihood function of f and logarithm of prior distribution [17]. Since the underlying likelihood function is assumed to be in a Poisson form, we come up with the following optimization model for SPECT reconstruction [12]:

$$f_{\star} = \arg \min_{f \geq 0} \{ \langle Af, \mathbf{1} \rangle - \langle \ln(Af + \gamma), g \rangle + \lambda U(f) \}. \quad (2)$$

The data fidelity function $F := \langle A \cdot, \mathbf{1} \rangle - \langle \ln(A \cdot + \gamma), g \rangle$ is the Kullback-Leibler (KL) divergence. The penalty function λU is introduced to impose desired smoothness on the estimate. Here, λ is a positive penalty-weight, and U is a real-valued energy function. Since this work solely discusses the reconstruction of piecewise constant phantom with sharp edges, we choose U as the total variation (TV) semi-norm. The advantage of using TV as a penalty function, over some other common regularization approaches that rely on various forms of the quadratic energy function, is that it is less sensitive to outliers and thus better preserves sharp edges in the estimated activity distribution. The limitations of TV include its non-differentiability and “staircase” artifacts. The former problem was tackled in the derivation of PAPA [12]. The latter one can be ameliorated by inclusion of higher-order derivative regularization terms in the objective function, see e.g. [13]. We emphasize that we have implemented an advanced approach to the nondifferentiable optimization problem, and our method does not require introduction of an *ad hoc* parameter as has been done in the past [6] to deal with non-differentiability.

The constraint that $f \geq 0$ is required, because the image f has all non-negative components.

2.2. Optimization approach

In this subsection, we recall our previously proposed iterative scheme for SPECT reconstruction with the nondifferentiable regularizer. For the convenience of exposition, we consider a typical SPECT image as a $p \times p \times q$ hypermatrix and treat this hypermatrix as a vector in $\mathbb{R}^{p^2 q}$ in such a way that the ijk th entry of the image matrix corresponds to the $(i + (j - 1)p + (k - 1)p^2)$ th component of the vector. In the current context, we reserve d for $p^2 q$. For an image $f \in \mathbb{R}^d$, the isotropic total variation (ITV) [13] of the image has the form $\phi(Bf)$. Here, B is a $3d \times d$ first-order difference matrix defined, through the identity matrix I , the backward difference matrix D and the notion of Kronecker tensor product $\otimes$, as

$$B := \begin{bmatrix} I_q \otimes I_p \otimes D_p \\ I_q \otimes D_p \otimes I_p \\ D_q \otimes I_p \otimes I_p \end{bmatrix} \text{ with } D := \begin{bmatrix} 0 & & & \\ -1 & 1 & & \\ & \ddots & \ddots & \\ & & -1 & 1 \end{bmatrix}.$$

The convex function $\varphi: \mathbb{R}^{3d} \rightarrow \mathbb{R}$ is defined at $z \in \mathbb{R}^{3d}$ as

$$\varphi(Z) := \sum_{i=1}^d \left\| [Z_i, Z_{d+i}, Z_{2d+i}]^\top \right\|.$$

With these preparations, we recall the algorithmic development in Krol et al. [12] and propose an iteration scheme for penalized ML SPECT reconstruction, now with the ITV regularizer,

$$\begin{cases} h^{(k)} := P_+(f^{(k)} - S \nabla F(f^{(k)}) - \mu S B^\top b^{(k)}), \\ b^{(k+1)} = (\mathcal{J} - \text{prox}_{(\lambda/\mu)\varphi})(b^{(k)} + B h^{(k)}), \\ f^{(k+1)} = P_+(f^{(k)} - S \nabla F(f^{(k)}) - \mu S B^\top b^{(k+1)}). \end{cases} \quad (3)$$

In scheme (3) $b^{(k)} \in \mathbb{R}^{3d}$ are dual iterates defined in the first-order difference transform domain. They are truncated by the soft thresholding function at each iteration, and $B^\top b^{(k)}$ resemble the noise in the image domain. In addition, S is the $d \times d$ diagonal, positive-definite preconditioning matrix that accelerates the resultant algorithm; and μ is a positive parameter. Motivated by the classical MLEM algorithm [18], we choose the preconditioning matrix S as the diagonal matrix $S^{(k)} := \text{diag}(f^{(k)}/A^\top \mathbf{1})$ at the k th iteration. In this way, S is updated once a new primal iterate $f^{(k)}$ is available.

Implementation of (3) also requires the availability of explicit formulas for P_+ and $\text{prox}_{(\lambda/\mu)\varphi}$. The operator P_+ is a projection onto the first octant. Specifically, for any $x \in \mathbb{R}^d$, we have $(P_+(x))_i = \max\{x_i, 0\}$. Moreover, recalling Example 2.5 in Micchelli et al. [11], we can calculate the components of the vector $y := \text{prox}_{(\lambda/\mu)\varphi}(z)$ by

$$[y_i, y_{d+i}, y_{2d+i}]^\top = \max \left\{ \left\| [z_i, z_{d+i}, z_{2d+i}]^\top \right\| - \frac{\lambda}{\mu}, 0 \right\} \frac{[z_i, z_{d+i}, z_{2d+i}]^\top}{\left\| [z_i, z_{d+i}, z_{2d+i}]^\top \right\|}, \quad (4)$$

$$i = 1, 2, \dots, d.$$

The above two explicit formulas are convenient for numerical evaluation in the sense that no additional optimization problems need to be solved.

3. Simulation studies

3.1. Simulated SPECT data

We used the Monte Carlo simulation software package (SIMIND [19]) to obtain the fan-beam (focal length 43.1 cm) SPECT data (consisting of 120 projection views in a 128×64 -dimensional detector matrix with 3.56 mm detector element size, and 2.2 mm reconstruction space voxel size) of piecewise constant phantom. We used an 18% energy window centered at 140 keV. Only primary photons and first-order scattered photons within this energy

window were considered. We simulated a uniform cylinder of diameter 20.8 cm and length 14.08 cm, containing uniform hot and cold spheres with sharp edges: six hot spheres in one transaxial plane at the same radial distance with relative sphere-to-background activity ratio of 2:1 and central cross-section areas ranging from 0.58 cm² for Sphere 6 to 4.26 cm² for Sphere 1 [Fig. 1(a)]; and six cold spheres (zero activity) in one transaxial plane with identical locations and sizes as hot spheres [Fig. 1(b)]. In addition, for lesion detectability comparison, we simulated fan-beam SPECT data for a reference cylinder with uniform background activity only [Fig. 1(c)], using the same geometry. In order to suppress photon-flux fluctuations, we simulated a total of 9.8×10^8 photon histories. The Monte Carlo-simulated projection images so obtained were multiplied by appropriate constants to reach a total of 4.2×10^6 and 8.4×10^6 counts in 120 views for the high-noise and low-noise data, respectively. Based on these nearly-noiseless projection data, we used a Poisson random number generator to create 100 different noise realizations for each phantom (400 data sets in total).

3.2. Reconstruction methods

3.2.1. Expectation maximization algorithm with Gaussian post-filter (GPF-EM)

—An ordered-subset version of the ML-EM algorithm is widely used in clinical SPECT reconstruction [14,15]. The aim of ML-EM is to find an image $f_\star$ that has the greatest statistical consistency with the observed data. For Poisson-distributed data (1), the underlying optimization model reads:

$$f_\star = \arg \min_{f \geq 0} \{ \langle Af, \mathbf{1} \rangle - \langle \ln (Af + \gamma), g \rangle \}. \quad (5)$$

The ML-EM algorithm iteratively solves model (5) in the following form:

$$f^{(k+1)} = \text{diag} \left(\frac{f^{(k)}}{A^T \mathbf{1}} \right) A^T \left(\frac{g}{Af^{(k)} + \gamma} \right). \quad (6)$$

It is well known that as the iterations of unbiased ML-EM proceed, the spatial resolution of reconstructed images increases accompanied by noise increase. In order to suppress the unacceptably high image noise in such an estimator, one needs to introduce a certain amount of bias into the reconstructed image in exchange. This is accomplished by prematurely stopping the algorithm before it actually reaches the ML solution and by post-smoothing. Note that stopping iterations too early might lead to loss of spatial resolution. Therefore, one needs to experimentally determine the stopping criterion for ML-EM, with the optimal tradeoff between spatial resolution and noise. Based on the qualitative assessment of reconstructed images, we stop ML-EM at 50th iteration and apply a 3D Gaussian post-filter to reduce the image noise and edge artifacts, since this post-filter ties us back to the clinical practice.

3.2.2. Expectation maximization algorithm with TV post-filter (TVPF-EM)—

Gaussian post-filtering results in a smoothing process irrespective of piecewise constant nature of the investigated phantom, and hence may not be an apt benchmark under the scope of this work. The well-studied Rudin–Osher–Fatemi (ROF) model [4] can efficiently suppress the image noise, meanwhile preserving sharp edges and locally constant regions. Therefore, it is best suited for the post-reconstruction smoothing of piecewise constant phantom. Indeed, the ROF model amounts to the following variational formulation:

$$f_{\star} = \arg \min_{f \in \mathbb{R}^d} \left\{ \frac{1}{2} \|f - f^{\infty}\|^2 + \lambda \varphi(Bf) \right\} \quad (7)$$

with f^{∞} the output of $f^{(k)}$ from the ML-EM iteration scheme (6). Remark that in statistical estimation problems where the likelihood function is unknown, one can use the least-squares principle to measure the consistency between the observed data and the estimate, which naturally leads to the quadratic fidelity function. The penalty function is chosen as the ITV regularizer $\lambda \varphi \circ B$ with λ a positive penalty-weight.

In order to reduce the overall computational load and meet the real-time reconstruction requirement, we need a fast solver for model (7). Micchelli et al. developed a theoretically solid and numerically efficient algorithm – the fixed-point algorithm based on the proximity operator with ITV (FP²O-ITV-B) for solving the ROF model in [11]. We shall stop ML-EM at 50th iteration and apply the FP²O-ITV-B for the post-reconstruction TV-denoising model (7). Accordingly, given any initial $v^{(0)} \in \mathbb{R}^{3d}$, the update equation reads:

$$v^{(k+1)} = \left(\mathcal{J} - \text{prox}_{(\lambda/\mu)\varphi} \right) (Bf^{\infty} + (I - \mu BB^T)v^{(k)}). \quad (8)$$

Write the output of $v^{(k)}$ from the above loop as v^{∞} and we can compute the solution of model (7) as $f_{\star} = f^{\infty} - \mu B^T v^{\infty}$. Readers may refer to [11] for details.

3.2.3. Forward-backward splitting algorithm with nested EM-TV iteration (FB-EM-TV)—

The FB-EM-TV method was recently introduced to solve emission tomography reconstruction problem (2) [7,8]. Its nested iteration scheme can be written as follows:

$$\begin{aligned} \text{EM Step: } f^{(k+\frac{1}{2})} &= \text{diag} \left(\frac{f^{(k)}}{A^T \mathbf{1}} \right) A^T \left(\frac{g}{A f^{(k)} + \gamma} \right), \\ \text{TV Step: } f^{(k+1)} &= \arg \min_{f \in \mathbb{R}^d} \left\{ \frac{1}{2} \left\| f - f^{(k+\frac{1}{2})} \right\|^2, \text{diag} \left(\frac{A^T \mathbf{1}}{f^{(k)}} \right) \left(f - f^{(k+\frac{1}{2})} \right) \right\} + \lambda \varphi(Bf) \end{aligned} \quad (9)$$

This iteration scheme consists of two alternatively performed steps: the EM step and the TV correction step. The EM step is identical to the ML-EM iteration step (6). The TV correction

step requires solving a modified ROF model exactly and is carried out by exploiting an existing numerical scheme for the ROF model. We followed the suggestion made in [7] and used the Chambolle algorithm [20] to solve the modified ROF model. Indeed, by applying Fermat's rule to model (9), the solution $f^{(k+1)}$ of (9) is simply given by

$$f^{(k+1)} = f^{(k+\frac{1}{2})} - \lambda \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T \nu^\star. \quad (10)$$

Here, $\nu^\star$ is a solution of the dual problem with a nonlinear constraint:

$$\begin{cases} \min_{\nu \in \mathbb{R}^{3d}} \left\{ \frac{1}{2} \left\| \lambda \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T \nu - f^{(k+\frac{1}{2})}, \text{diag}\left(\frac{A^T \mathbf{1}}{f^{(k)}}\right) (\lambda \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T \nu - f^{(k+\frac{1}{2})}) \right\|^2 \right\} \\ \text{s.t. } \left\| [\nu_i, \nu_{d+i}, \nu_{2d+i}]^T \right\|^2 - 1 \leq 0, \forall i = 1, 2, \dots, d. \end{cases} \quad (11)$$

Similar to [20], Sawatzky et al. derived a semi-implicit gradient descent algorithm to solve model (11): given any initial $\nu^{(0)} \in \mathbb{R}^{3d}$, for any $l = 0, 1, \dots$, they computed

$$\nu^{(l+1)} = \frac{\nu^{(l)} - \tau B \left(\lambda \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T \nu^{(l)} - f^{(k+\frac{1}{2})} \right)}{1 + \tau \left\| B \left(\lambda \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T \nu^{(l)} - f^{(k+\frac{1}{2})} \right) \right\|} \quad (12)$$

with the damping parameter τ constrained by $0 < \tau < 1/(4\lambda \left\| \frac{f^{(k)}}{A^T \mathbf{1}} \right\|_\infty)$. The iteration number of

the sub-iteration (12) is a crucial factor for developing efficient numerical schemes.

Although more sub-iterations may produce a stably-convergent solution, the related computational load would be very heavy. In practice, given that the resulting ν from the previous TV correction step is a reasonable initial value for solving (11), the total iterations of the updating scheme (12) could be reduced significantly. A straightforward choice of the sub-iteration number would be 1. Under these circumstances, the iteration scheme of FB-EM-TV reduces to

$$\begin{cases} h^{(k)} := f^{(k+\frac{1}{2})} - \lambda \tau \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T b^{(k)}, \\ b^{(k+1)} = \frac{b^{(k)} + B h^{(k)}}{1 + \tau \|B h^{(k)}\|}, \\ f^{(k+1)} = f^{(k+\frac{1}{2})} - \lambda \tau \text{diag}\left(\frac{f^{(k)}}{A^T \mathbf{1}}\right) B^T b^{(k+1)} \end{cases} \quad (13)$$

with $b^{(k)} := v^{(k)}/\tau$. We can easily verify that $\nabla F(f) = A^T \left(\mathbf{1} - \frac{g}{Af + \gamma} \right)$, and thus have

$f^{(k+\frac{1}{2})} = f^{(k)} - S^{(k)} \nabla F(f^{(k)})$. In this fashion, the update equations for primal variables (i.e. $h^{(k)}$ and $b^{(k+1)}$) in scheme (13) are almost identical to those in scheme (3) except that TV-PAPA involves a projection onto the first octant at each primal update. As for the dual update, both iteration schemes provide possible ways for solving model (11) and perform sub-iteration once at each complete outer iteration, but they act differently (see comparison between the FP²O-ITV-B and the Chambolle algorithm in [11]). Indeed, substituting Eq. (4) into (3) leads to an explicit formula for the dual update:

$$b^{(k+1)} = \frac{\min \left\{ \frac{\lambda}{\mu}, \|b^{(k)} + B h^{(k)}\| \right\} (b^{(k)} + B h^{(k)})}{\|b^{(k)} + B h^{(k)}\|}. \quad (14)$$

Both (14) and the dual update equation in scheme (13) are non-expansive with respect to $b^{(k)} + B h^{(k)}$, depending on different parameters.

In summary, TV-PAPA and FB-EM-TV are developed to solve the same optimization model (2), and both share very similar iteration schemes. Therefore, we expect comparable reconstruction qualities and computational performances for the two competing methods. Finally, based on the qualitative assessment of reconstructed images, we stop the scheme (13) at 100th iteration.

3.2.4. Preconditioned alternating projection algorithm with TV regularization

(TV-PAPA)—Because the convex function ϕ that defines the ITV regularizer is nondifferentiable, conventional gradient-type and expectation maximization-type algorithms that require information on the gradient of the penalty function cannot solve the ITV-regularized optimization problem (2). The proposed TV-PAPA does not require any kind of smoothing technique to deal with nondifferentiability and can iteratively solve problem (2) based on its fixed-point characterization [12]. Further, the original nested iteration scheme of FB-EM-TV requires an exact solution of a modified ROF model at each outer iteration, which makes the algorithm intractable. In practice, we may perform the sub-iteration of FB-EM-TV finite times or even more time-saving, once. Such approximation schemes (e.g. scheme (13)) cannot guarantee the theoretical convergence [8]. In contrast, the TV-PAPA

does not need to perform an exact inner-optimization and it leads to a more practical algorithm. Besides, it is guaranteed to converge, both theoretically and numerically. We stop the TV-PAPA at 100th iteration.

3.3. Parameters

The TV-PAPA method required estimation of two parameters: λ and μ . We set

$$\mu = 1/(2\lambda\|B\|_2^2\| \frac{f^{(k)}}{A^T 1} \|_\infty) \text{ at the } k\text{th iteration as suggested in [12]. The optimal value of}$$

penalty-weight λ was obtained by performing a set of trial reconstructions with λ ranging from 10^{-4} to 1. Three observers qualitatively considered the dependence of spatial resolution, contrast and image noise on λ . Indeed, each observer independently and subjectively balanced the tradeoff among the above three metrics, and selected the best λ for each noise level. The penalty-weights selected by three observers were averaged and the average values were used as the optimal parameters: $\lambda = 0.028$ and 0.0057 for high- and low-noise simulated data, respectively.

As for the FB-EM-TV method, we followed the aforementioned procedure and selected $\lambda = 0.033$ and 0.0053 for high- and low-noise data, respectively.

The TVPF-EM method required determination of a positive penalty-weight when solving the post-reconstruction TV-denoising model (7). The above procedure applied to this case and determined that $\lambda = 0.05$ and 0.007 for high- and low-noise data, respectively.

For images reconstructed with GPF-EM, we performed another set of trial reconstructions with the full width at half maximum (FWHM) of the Gaussian blurring kernel ranging from 0.5 mm to 6.1 mm, and repeated the proposed parameter determination procedure by multiple observers. In this way, we determined the optimal FWHM to be 3.1 mm and 0.6 mm for high- and low-noise data, respectively.

3.4. Image degradation compensation

The distance-dependent spatial resolution, attenuation and sensitivity in reconstructions were corrected using model-based compensation methods for calculating the system matrix A . Only the first-order scatter present in the simulated SPECT data was approximately corrected by using the broad-beam attenuation coefficient $\mu = 0.12 \text{ cm}^{-1}$ at 140 keV .

3.5. Quantification of reconstruction

In order to compare the performance of TV-PAPA with those of FB-EM-TV and TVPF-EM, we evaluated the following metrics suitable for assessment of nonlinear and shift-variant SPECT imaging systems [21,22].

3.5.1. Ensemble noise—Ensemble noise provides a useful measure of image noise across multiple noise realizations. For the k th region of interest ROI_k ($k = 1, 2, \dots, K$ and K is the total number of background ROIs), the ensemble noise is defined as the variance of ROI mean activities $m_{r,k}$ over multiple independent noise realizations $r = 1, 2, \dots, R$ [22]:

$$\sigma_{\text{ensemble},k}^2 = \frac{1}{R-1} \sum_{r=1}^R (m_{r,k} - \bar{m}_k)^2, \quad (15)$$

where $\bar{m}_k = \frac{1}{R} \sum_{r=1}^R m_{r,k}$ is the average of mean activities in ROI_k over R noise realizations and $\sigma_{\text{ensemble},k}^2$ is defined for each ROI_k. We further averaged this statistic over the K background ROIs and obtained the final background ensemble variance

$$\sigma_{\text{ensemble},k}^2 = \frac{1}{K} \sum_{K=1}^K \sigma_{\text{ensemble},k}^2$$

3.5.2. Ensemble voxel variance—Another commonly used metric for noise quantification is the ensemble voxel variance, which is defined for a given voxel i across multiple independent noise realizations $r = 1, 2, \dots, R$ as

$$\sigma_{0i}^2 = \frac{1}{R-1} \sum_{r=1}^R (f_{ir} - \bar{f}_i)^2. \quad (16)$$

Here, f_{ir} is the reconstructed activity for voxel i at noise realization r ; R is the number of total noise realizations, and $\bar{f}_i = \frac{1}{R} \sum_{r=1}^R f_{ir}$ is the averaged activity for voxel i over realizations. Definition (16) applies to a single voxel and hence a variance image can be generated voxel-wise.

3.5.3. Local noise power spectrum (LNPS)—Following the approach described in [23], we characterized the noise performance of investigated reconstruction methods by means of the normalized LNPS. The LNPS in [23] is defined for a selected ROI as the mean of the Fourier transforms of the reconstructed images with the Fourier transform of the average reconstructed image subtracted. This metric has been used to evaluate background noise properties in SPECT [21,24] and PET [22] reconstructions, as well as in the context of CT system [25]. A small ROI (a square of 16 pixels by 16 pixels) in the center of a transaxial cross-section of the reconstructed reference cylinder was selected for the computations.

3.5.4. Detectability of hot and cold spheres—We applied the channelized Hotelling observer (CHO), as described in [26], to quantify the detectability of simulated lesions (hot and cold spheres with uniform activities). We used four non-overlapping and rotationally symmetric input channels (in spatial frequency domain) and modeled the internal observer noise [27,28]. A total of 200 noise realizations (100 for the uniform cylinder and 100 for the cylinder with spheres) were used for low- and high-noise simulated data reconstructed by TV-PAPA, FB-EM-TV, TVPF-EM and GPF-EM. The detection performance was assessed by the estimation of the areas under the receiver-operating characteristic (ROC) vs. penalty-weight/Gaussian FWHM curves.

3.5.5. Normalized mean square error (NMSE)—We used the NMSE to assess accuracy of reconstructions. The NMSE is a global image quality metric, which quantifies the normalized difference between the reconstructed activity f and the phantom (the ground truth) activity f_0 in the whole reconstruction space. It is defined by

$$\text{NMSE} = \frac{\sum_{i=1}^N (f_i - f_{0i})^2}{\sum_{i=1}^N f_{0i}^2}, \quad (17)$$

where f_i and f_{0i} are voxel activities in the reconstructed image and phantom, respectively, and N is the total number of voxels in the reconstruction space. We averaged Eq. (17) over multiple noise realizations and obtained the final NMSE estimate.

3.5.6. Mean lesion contrast—We calculated the mean lesion contrast using 2D ROIs in the transaxial cross-sections through the centers of hot or cold spheres. The target ROI matches the largest cross-section of the sphere. The background ROIs are of the same size as the target. We defined 10 of them distributed around the corresponding target and obtained their mean value. The absolute mean contrast is then defined as

$$C_a = \langle |T - B| \rangle, \quad (18)$$

where T is the mean activity in the target ROI (hot or cold sphere) for a given noise realization, B is the mean activity over 10 surrounding circular background ROIs for the same realization, and notation $\langle \cdot \rangle$ denotes the average over multiple independent noise realizations.

3.5.7. Best lesion contrast—We used spherical volumes-of-interest (VOIs) to calculate the best lesion contrast. The target VOI matches the volume of the uniform hot or cold sphere. The background VOIs are of the same size as the target. We selected 10 background VOIs around the corresponding target and calculated their mean activity. The absolute best contrast then reads

$$C_a^c = \langle |T^c - B| \rangle. \quad (19)$$

In the above equation, T^c is the maximum (resp. minimum) activity for a specific hot (resp. cold) target, and B is the mean activity averaged over 10 spherical background VOIs.

3.5.8. Contrast recovery coefficient—The contrast recovery coefficient (CRC) provides a useful measure of quantitative accuracy of reconstruction for the selected VOIs and it quantifies directly the partial volume effect. CRC for hot sphere is defined as

$$CRC_{\text{hot}} = \frac{\text{count}_{\text{hot}}/\text{count}_{\text{bkg}} - 1}{R - 1}, \quad (20)$$

where $\text{count}_{\text{hot}}$ and $\text{count}_{\text{bkg}}$ denote the mean numbers of counts per voxel in target and background VOIs, respectively, and R is the true sphere-to-background activity concentration ratio. For cold spheres, we define CRC as follows:

$$CRC_{\text{cold}} = 1 - \frac{\text{count}_{\text{cold}}}{\text{count}_{\text{bkg}}}. \quad (21)$$

In practice, CRC is always smaller than 1 and a higher CRC value corresponds to more accurate reconstruction for the given VOI.

4. Results

4.1. Reconstructed images

Fig. 2 shows examples of hot and cold spheres reconstructed for the same noise realization using the four investigated methods with optimal parameters. Horizontal line profiles passing through the centers of transaxial cross-sections of reconstructed (Fig. 2) or ground truth (Fig. 1) spheres are shown in Figs. 3(a) and (b) for hot and cold spheres, respectively. We observe that the image quality, including lesion contrast and spatial resolution, and the noise texture are very similar in the TV-PAPA and FB-EM-TV reconstructions. The benchmark TVPF-EM reconstructed noisier images with significantly different noise texture and worse spatial resolution. The GPF-EM reconstructions have the noisiest appearance and the worst spatial resolution. This qualitative comparison confirms the visual superiority of TV-PAPA and FB-EM-TV over TVPF-EM, not to mention GPF-EM, on reconstruction of piecewise constant phantom.

4.2. Image quality analysis

4.2.1. Normalized mean square error—The plots of NMSE (17) vs. iteration number are shown in Fig. 1 in the Supplementary Material. Despite its insensitivity to noise-resolution tradeoff, NMSE still provides a reasonable estimate of reconstruction accuracy. The plots show that regardless of iteration number or noise level, TV-PAPA and FB-EM-TV consistently produce comparable NMSE that is significantly smaller than the GPF-EM. For the low-noise data the NMSE for TV-PAPA is slightly smaller than that for FB-EM-TV, while for the high-noise data one reaches an opposite conclusion. The reason is that in the low-noise case, we selected a slightly larger penalty-weight λ for TV-PAPA, as compared to FB-EM-TV. A larger penalty-weight, within a reasonable parameter range, leads to a higher degree of noise suppression and more cartoon-like reconstructed image. As a result, a smaller NMSE is obtained for the piecewise constant nature of the investigated phantom. A similar analysis applies to the reconstructions from high-noise data, noting that under these circumstances the observer study determined a larger penalty-weight for FB-EM-TV.

4.2.2. Image noise performance—The LNPS images reconstructed using the four investigated methods for two sets of simulated SPECT data are shown in Fig. 2 in the Supplementary Material. The average radial profiles obtained for 36 azimuth angles (every 10°) are shown in Fig. 4. We observe that in the low-noise case, LNPS for TV-PAPA has somewhat lower mean and maximum amplitudes, as compared to FB-EM-TV. While in the high-noise case, TV-PAPA exhibits marginally higher amplitudes than FB-EM-TV (Table 1). This is because in the high-noise case the penalty-weight for TV-PAPA is smaller than that for FB-EM-TV, which leads to a slightly lower degree of image noise suppression for the former method.

The benchmark TVPF-EM produced lower mean and maximum LNPS amplitudes than GPF-EM. Both TV-PAPA and FB-EM-TV suppressed the local noise spectrum spatial frequency components on average by a factor of at least 2 and 43 for the low- and high-noise data, respectively, as compared to the benchmark TVPF-EM. The noise spectrum suppression increased to a factor of 6 and 71 for two data sets when comparing the two Bayesian-TV methods with GPF-EM. We further note that the maxima of LNPS for TVPF-EM and GPF-EM are at higher spatial frequencies.

4.2.3. Ensemble noise—The calculated background ensemble variances vs. iteration numbers are shown in Fig. 5. They were obtained using 100 noise realizations and a total of 120 circular ROIs: 60 ROIs centered at slices 21 to 25, and the other 60 centered at slices 40 to 44. We note that slices 23 and 42 are the central cross-sections of hot and cold spheres, respectively. The diameters of these ROIs are equal to 10 pixels. We observe that the TV-PAPA and FB-EM-TV performed comparably. Both Bayesian-TV methods outperformed the benchmark TVPF-EM, and significantly outperformed GPF-EM.

4.2.4. Ensemble voxel variance—The variance images obtained for the reconstructed hot and cold spheres across 100 noise realizations are shown in Fig. 6. We observe very different appearances of variance images for the benchmark TVPF-EM from the two Bayesian-TV methods, as indicated by the line profiles in Fig. 3 in the Supplementary Material. The amplitudes of voxel variances for TV-PAPA and FB-EM-TV are comparable. They exhibit very low noise levels in the background. The TVPF-EM produced higher ensemble voxel variances in the background, and the GPF-EM much higher across the whole reconstructed images (except for the cold spheres), as compared to the two Bayesian-TV methods. In the variance images generated by TV-PAPA and FB-EM-TV, we observe edge artifacts, appearing as ring-shaped overshoot due to the circles and similar to the ones observed for PET reconstructions [22]. This effect is usually referred to as the Gibbs phenomenon and has an intuitive mathematical interpretation: when we use a Fourier series with finite number of terms to approximate a discontinuous function, overshoots occur at the discontinuity points. The Bayesian-TV methods allow preservation of sharp edges (discontinuities), and thus introduce overshoots at the edges. Remark that for spheres of sufficiently small size, the edge artifacts merge to peaks.

4.2.5. CHO lesion detectability—Visual examination of reconstructed images for one noise realization (Fig. 2) indicates that the simulated lesions (hot and cold spheres) exhibit similar conspicuity for TV-PAPA and FB-EM-TV that is higher than the benchmark TVPF-

EM, and much higher than GPF-EM. This is confirmed by the CHO studies of the reconstructed images. We found comparable CHO detectability indices for TV-PAPA and FB-EM-TV, followed by TVPF-EM and GPF-EM (Fig. 7). The former three methods are superior to the later one, because the TV regularizer has better noise suppression ability and consists with the piecewise constant nature of the investigated phantom. Moreover, the Bayesian-TV reconstruction methods perform even better than the TV post-filtering method. Finally, the CHO detectability is a monotone increasing function of the lesion size.

4.2.6. Mean and best contrast for lesions—We calculated the mean (resp. best) contrast for simulated lesions over 100 noise realizations using circular ROIs (resp. spherical VOIs). The absolute mean contrast for hot and cold spheres reconstructed by TV-PAPA and FB-EM-TV at the 100th iteration, and by TVPF-EM (with 100 iterations of FP²O-ITV-B) and GPF-EM at the 50th iteration are presented in Table 2. And Table 3 collects the corresponding values of absolute best contrast. We observe that regardless of the lesion size or noise level, TV-PAPA and FB-EM-TV performed comparably in terms of both contrast, and that both contrast decrease as lesion shrinks. A closer look at the metric values, together with the parameter selection in Section 3.3, confirm that heavier TV regularization leads to increased loss of contrast. In some cases, GPF-EM produced higher contrast, especially for smaller lesions. The benchmark TVPF-EM compromised lesion contrast for better noise suppression, and performed worst in this category.

4.2.7. Contrast recovery coefficient—We calculated the CRCs of simulated lesions for one noise realization using spherical VOIs (Figs. 4 and 5 in the Supplementary Material). We observe that TV-PAPA and FB-EM-TV produced comparable CRC values at comparable convergence speed. Under the predetermined stopping criteria (100th iteration for TV-PAPA and FB-EM-TV, and 50th iteration for TVPF-EM and GPF-EM), GPF-EM produced marginally higher CRCs than Bayesian-TV methods for the smallest lesions (spheres 5 and 6). Still, TVPF-EM presented the lowest CRCs among the four competing methods.

4.2.8. Convergence speed and computational time—Table 4 shows the number of complete iterations used and the CPU time (units: second) expended by three iteration schemes for reconstruction of the high-noise simulated data of spheres phantom. The relative error we used in calculation is defined as

$$tol: = \|f^{(k)} - f^{(k+1)}\|_2 / \|f^{(k+1)}\|_2. \quad (22)$$

From Table 4 we conclude that, under the same stopping criteria, TV-PAPA is comparable to FB-EM-TV and both are better than the ML-EM iteration scheme in terms of both convergence speed and computational time. The relative error *tol* vs. iteration number is shown in Fig. 6 in the Supplementary Material. We observe that ML-EM cannot reach the relative error level below 10^{-3} (see entries marked by dashes in Table 4).

4.2.9. Parameter selection—We show in Fig. 8 the parameter tolerance ranges of TV-PAPA, TVPF-EM and GPF-EM for a sequence of information density (defined as the total

number of counts in the SPECT data divided by the image support volume in voxels [29,30]). We determined feasible upper and lower bounds, and optimal values of involved parameters both qualitatively and quantitatively. Indeed, for each level of information density, we performed three sets of trial reconstructions with varying Bayesian-TV penalty-weights, TV post-filtering penalty-weights or Gaussian post-filtering FWHMs. And we chose feasible lower bounds by decreasing the involved parameters until the image noise exceeded a predefined threshold. As for feasible upper bound determination, we qualitatively analyzed the dependence of spatial resolution and contrast on the involved parameters, and selected the maximum ones prior to significant loss of the above two metrics. The observer-optimized parameters were obtained following the procedure described in Section 3.3. We observe that TV-PAPA has wider parameter tolerance ranges at higher levels of information density, and hence is more tolerant to the involved parameter, as compared to the other two post-filtering methods. Moreover, both observer-optimized and NMSE-optimized parameters vs. the information density can be well fitted by power-law functions, as suggested in refs. [29,30]. This observation points toward simplified parameter selection for the reconstruction methods.

Remark that a plethora of methods for the selection of the regularization parameter has been proposed in the case of Tikhonov theory, the most popular being the discrepancy principle. In the case of Poisson data only a few have been proposed so far [31,32], including the crossing model and the I -divergence constrained minimization model. We start from the numerical point of view, and reveal in Fig. 8 how our selected optimal parameters vary with the information density, out of existing sampling points. This simulation study gives us some guidance in the parameter selection at more levels of information density.

4.3. Comparison of realistic simulated case

To evaluate the performance of the competing methods in a realistic setting, we simulated a brain phantom (Fig. 7 in the Supplementary Material), which was taken from a slice of a SPECT brain scan and was subsequently denoised using the high-order TV regularizer [13]. The simulated data was reconstructed using the four investigated methods. The reconstructed images are shown in Fig. 9, with associated vertical line profiles through the hot lesion shown in Fig. 10. We observe that the TV-type methods can better suppress image noise and preserve spatial resolution, as compared to GPF-EM. The Bayesian-TV methods suppress image oscillation better than the benchmark TVPF-EM, with only limited loss of lesion contrast.

5. Summary and conclusions

In the present work, we compared the performance of two novel penalized likelihood reconstruction methods that might allow clinical work with lower administered activity than presently possible, thus conceivably allow lower radiation exposure to patients in nuclear medicine. Both methods explored the total variation (TV) regularization. The major advantages of TV lie in its preservation of high frequency components of the reconstructed radiopharmaceutical distribution and in efficient suppression of image noise.

We compared the performance of the proposed TV-PAPA to that of FB-EM-TV. The two methods were developed based on different theoretical foundation. The conventional maximum likelihood expectation maximization (ML-EM) algorithm with TV post-filter (TVPF-EM) was used as a benchmark. We further compared the three TV-type reconstruction methods with the clinically-used ML-EM algorithm with Gaussian post-filter (GPF-EM).

Monte Carlo-simulated fan-beam SPECT data were generated for two piecewise constant phantoms: a water cylinder with uniform warm background containing uniform hot and cold spheres of various sizes, and a reference cylinder with identical uniform background only. Such simple phantoms are best suited for evaluation of the performance of TV regularization in the penalized likelihood reconstruction.

We assessed the reconstructed images of four methods qualitatively and quantitatively, via evaluating their reconstruction accuracy, noise suppression, lesion detectability, contrast preservation and convergence speed. We observed comparable performance for both Bayesian-TV reconstruction methods in every category investigated. They outperformed the benchmark TVPF-EM, and significantly outperformed GPF-EM in terms of hot and cold lesions detectability, image noise suppression and reconstruction accuracy. They converged faster than the ML-EM algorithm. The only advantages that we found for GPF-EM are somewhat higher contrast and CRC attained for the smallest simulated lesions, which is expected due to the greater noise in these reconstructed images.

We established that the feasible upper and lower bounds, and optimal values (in the sense of observer selection and NMSE) of involved parameters vs. the information density approximately followed power laws. Therefore, we conclude that one can predict optimal parameters at the desired levels of information density based on prior knowledge. This would have important consequences on the potential clinical applications of TV-PAPA.

In sum, we conclude that even though TV-PAPA and FB-EM-TV were derived within different theoretical frameworks, they exhibited very similar tomographic performance for the investigated piecewise constant phantom and anthropomorphic brain phantom, and all the observed differences can be explained by differences in penalty-weights used. We have also shown that both Bayesian-TV methods outperformed the benchmark TVPF-EM and the clinically-used GPF-EM for low- and high-noise simulated data in terms of most categories, with exception of minor contrast and CRC loss for the smallest simulated lesions. These findings are also confirmed by qualitative analysis of the reconstructed anthropomorphic images. Therefore, the TV-PAPA and FB-EM-TV methods are good candidates for applications aiming at lowering the effective radiation dose in clinical SPECT studies and are definitely worth further investigation to this end.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research is supported in part by the Special Project on High-performance Computing under the National Key R&D Program (No. 2016YFB0200602) and by the Natural Science Foundation of China under grants 11601537, 11471013 and 91530117. This work is supported in part by Award 5-28527 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and the NIH Roadmap for Medical Research, and by the Center of Emerging and Innovative Sciences (CEIS), a NYSTAR designated Center for Advanced Technology. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health. This work is supported in part by Carol M. Baldwin Breast Cancer Research Award. This research is also supported in part by the MSK Cancer Center Support Grant/Core Grant P30 CA008748.

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Fig. 1.

Transaxial cross-sections through piecewise constant phantom containing: (a) uniform warm background with six hot spheres with uniform activity and with sphereto-background activity ratio of 2:1; (b) uniform warm background with six uniform cold spheres with zero activity. (c) Transaxial cross-section through the uniform attenuation map. The line segments indicate locations of the line profiles.

Fig. 2. Transaxial cross-sections through the reconstructed images obtained for the same noise realization using optimal parameters. Images in the upper and lower rows correspond, respectively, to hot and cold spheres.

Fig. 3.

Horizontal one channel wide line profiles through centers of reconstructed images shown in Fig. 2: (a) hot spheres; (b) cold spheres. Spheres with diameters 13.2 and 22 mm are centered at pixels 38 and 89, respectively. The location of horizontal line profile is indicated in Fig. 1.

Fig. 4.

Average radial profiles through the local noise power spectra obtained for the four methods and two sets of simulated data. The insets show magnified plots for TV-PAPA and FB-EM-TV. Radial profiles were obtained for every 10° . A total of 36 profiles were used for averaging. The Nyquist frequency is $1/0.44$ cycles/cm.

Fig. 5. Background ensemble variance vs. iteration number, calculated using the four investigated methods for low-noise simulated data.

Fig. 6.

Variance images of reconstructed hot (upper row) and cold (lower row) spheres from low-noise simulated data. All images were obtained by reconstruction of 100 noise realizations for the four investigated methods. The corresponding reconstructed images obtained for one noise realization are shown in Fig. 2.

Fig. 7.

CHO detectability indices of uniform spheres of various sizes for hot spheres with sphere-to-background activity ratio of 2 : 1 [(a) and (c)]; and cold spheres with zero activity [(b) and (d)]. Subfigures in the upper and lower rows correspond, respectively, to reconstructions of low-noise and high-noise simulated data. The solid lines connecting calculated data points are provided as visual aids.

Fig. 8.

Normalized Gaussian post-filtering FWHMs and penalty-weights as functions of information density for (a) GPF-EM, (b) TVPF-EM and (c) TV-PAPA, respectively. The power-law curve fits suggest simplified parameter selection for the three reconstruction methods.

Fig. 9.
Reconstructed images of the denoised brain phantom obtained by four investigated methods.

Fig. 10.
Vertical line profiles through the hot lesions in the reconstructed images of the brain phantom.

Table 1

Average and maximum amplitudes, and spatial frequencies corresponding to the maxima in amplitudes for LNPS obtained using TV-PAPA, FB-EM-TV, TVPF-EM and GPF-EM.

Method	GPF-EM	TVPF-EM	FB-EM-TV	TV-PAPA
<i>Low-noise simulated data</i>				
Average LNPS amplitude (arbitrary units)	17.8	6.8	3.0	2.4
Maximum LNPS amplitude (arbitrary units)	44.1	18.6	10.1	8.3
Spatial frequency corresponding to maximum LNPS amplitude (cm^{-1})	0.30	0.30	0.27	0.27
<i>High-noise simulated data</i>				
Average LNPS amplitude (arbitrary units)	0.5	0.3	0.004	0.007
Maximum LNPS amplitude (arbitrary units)	1.5	1.3	0.02	0.04
Spatial frequency corresponding to maximum LNPS amplitude (cm^{-1})	0.28	0.28	0.21	0.21

Table 2

The absolute mean contrast for hot and cold spheres reconstructed by four competing methods. Remark that in the high noise simulation case, the smallest 2 hot and cold spheres are smoothed away and hence out of consideration. These phenomena are marked by – in the table.

Lesion size	Sphere 1	Sphere 2	Sphere 3	Sphere 4	Sphere 5	Sphere 6
<i>Low-noise simulated hot sphere</i>						
TV-PAPA	28.4 ± 1.4	28.3 ± 2.0	25.0 ± 3.1	21.8 ± 3.4	12.8 ± 3.6	7.3 ± 3.4
FB-EM-TV	28.5 ± 1.4	28.4 ± 2.0	25.3 ± 3.2	22.2 ± 3.5	13.4 ± 3.7	7.8 ± 3.6
TVPF-EM	27.2 ± 1.2	25.3 ± 1.4	20.3 ± 1.9	17.7 ± 2.2	10.8 ± 2.1	7.3 ± 2.3
GPF-EM	28.8 ± 2.2	28.7 ± 2.6	26.2 ± 3.4	23.2 ± 3.8	16.2 ± 3.5	11.5 ± 3.8
<i>Low-noise simulated cold sphere</i>						
TV-PAPA	25.8 ± 0.9	23.7 ± 1.3	19.0 ± 1.9	17.3 ± 1.9	10.4 ± 3.0	5.8 ± 2.8
FB-EM-TV	25.6 ± 0.9	23.5 ± 1.2	18.9 ± 1.8	17.3 ± 1.8	10.6 ± 3.0	6.1 ± 2.8
TVPF-EM	22.0 ± 0.6	19.1 ± 0.8	14.3 ± 1.1	12.8 ± 1.0	8.3 ± 1.6	5.5 ± 1.7
GPF-EM	23.2 ± 0.8	21.3 ± 1.1	17.4 ± 1.5	16.3 ± 1.5	11.6 ± 2.5	8.6 ± 2.6
<i>High-noise simulated hot sphere</i>						
TV-PAPA	4.1 ± 0.4	3.6 ± 0.6	2.0 ± 0.9	1.7 ± 0.7	–	–
FB-EM-TV	4.0 ± 0.4	3.4 ± 0.5	1.7 ± 0.8	1.4 ± 0.6	–	–
TVPF-EM	3.9 ± 0.3	3.2 ± 0.3	2.1 ± 0.5	1.9 ± 0.5	–	–
GPF-EM	4.0 ± 0.3	3.4 ± 0.4	2.4 ± 0.5	2.2 ± 0.5	–	–
<i>High-noise simulated cold sphere</i>						
TV-PAPA	4.0 ± 0.3	3.2 ± 0.5	1.8 ± 0.8	1.4 ± 0.7	–	–
FB-EM-TV	3.9 ± 0.3	3.0 ± 0.5	1.5 ± 0.7	1.1 ± 0.6	–	–
TVPF-EM	3.2 ± 0.2	2.5 ± 0.3	1.5 ± 0.3	1.4 ± 0.4	–	–
GPF-EM	3.3 ± 0.2	2.6 ± 0.3	1.8 ± 0.3	1.6 ± 0.3	–	–

Table 3

The absolute best contrast for hot and cold spheres reconstructed by four competing methods. Remark that in the high noise simulation case, the smallest 2 hot and cold spheres are smoothed away and hence out of consideration. These phenomena are marked by – in the table.

Lesion size	Sphere 1	Sphere 2	Sphere 3	Sphere 4	Sphere 5	Sphere 6
<i>Low-noise simulated hot sphere</i>						
TV-PAPA	40.8 ±4.8	40.0 ±4.4	36.8 ±7.0	32.3 ±6.7	17.2 ±5.2	9.7 ±4.7
FB-EM-TV	41.8 ±5.1	41.0±4.6	38.0 ±7.3	33.4 ±7.0	18.2 ±5.5	10.5 ±5.0
TVPF-EM	40.4 ±2.6	38.6 ±3.2	30.3 ±3.6	26.7 ±3.9	14.7 ±2.7	10.2 ±2.7
GPF-EM	52.6 ±4.9	51.3 ±5.7	44.5 ±6.8	40.0 ± 7.2	25.6 ±4.9	18.4 ±5.0
<i>Low-noise simulated cold sphere</i>						
TV-PAPA	31.0 ±1.4	30.0 ±1.8	24.2 ±2.8	22.6 ±2.9	13.3 ±3.7	7.7 ±3.8
FB-EM-TV	30.6 ±1.2	29.2 ±1.6	23.9 ±2.5	22.4 ±2.7	13.6 ±3.6	8.2 ±3.7
TVPF-EM	27.4 ±0.9	24.9 ±1.1	19.0 ±1.5	17.5 ±1.4	11.0±1.7	7.8 ±1.8
GPF-EM	29.3 ± 1.0	27.6 ±1.2	23.0 ±1.8	22.0 ±1.9	16.0 ±2.3	12.6 ±2.7
<i>High-noise simulated hot sphere</i>						
TV-PAPA	5.3 ±0.9	4.7 ±1.0	2.7 ±1.2	2.2 ±1.0	–	–
FB-EM-TV	4.9 ±0.7	4.2 ±0.9	2.1 ±1.1	1.8 ±0.8	–	–
TVPF-EM	6.0 ±0.6	4.9 ±0.7	3.1 ±0.6	2.9 ±0.6	–	–
GPF-EM	6.3 ±0.7	5.4 ±0.7	3.7 ±0.7	3.4 ±0.7	–	–
<i>High-noise simulated cold sphere</i>						
TV-PAPA	4.8 ±0.5	4.0 ±0.7	2.4 ±1.1	2.0 ±0.9	–	–
FB-EM-TV	4.5 ±0.4	3.7 ±0.7	1.9 ±1.0	1.5 ±0.9	–	–
TVPF-EM	4.4 ±0.2	3.5 ±0.3	2.3 ±0.4	2.1 ±0.4	–	–
GPF-EM	4.4 ±0.3	3.6 ±0.3	2.5 ±0.4	2.3 ±0.4	–	–

Table 4

Comparison of the performance of ML-EM, FB-EM-TV and TV-PAPA for the high-noise simulated data of spheres phantom. The pair ($\cdot$; $\cdot$) represents the number of complete iterations and the CPU time (units: second) needed to achieve various relative error levels.

Iteration scheme	tol		
	10^{-1}	10^{-2}	10^{-3}
ML-EM	(4, 351.2)	(15, 1221.4)	(-, -)
FB-EM-TV	(4, 383.9)	(12, 1073.9)	(50, 4222.0)
TV-PAPA	(4, 364.4)	(13, 1110.3)	(52, 4156.3)