Performance Evaluation of an Iterative Image Reconstruction Algorithm for Positron Emission Tomography

Gabor T. Herman, Fellow, IEEE, and Dewey Odhner

Abstract—We discuss an image reconstruction method motivated by positron emission tomography (PET). The measurements tend to be noisy and so the reconstruction method should incorporate the statistical nature of the noise. We set up a discrete model to represent the physical situation and arrive at a nonlinear maximum a posteriori probability (MAP) formulation of the problem. Previously published iterative procedures for this maximization problem involve the solution of $10^3$ to $10^5$ coupled quadratic equations at each iterative step. In this paper an alternative iterative approach, which requires the solution of simple (not coupled) quadratic equations, is motivated and proposed. The method decomposes naturally for parallel computing. We also present a methodology which allows us to experimentally optimize an image reconstruction method for a specific medical task and to evaluate the relative efficacy of two reconstruction methods for a particular task in a manner which meets the high standards set by the methodology of statistical hypothesis testing. We illustrate this by comparing, in the area of PET, the new MAP algorithm to a method which maximizes likelihood and with two variants of the filtered backprojection method. We find that the relative performance of techniques is extremely task dependent, with the new method superior to the others from the point of view of two other PET-related figures of merit. In particular, we find that, in spite of the very noisy appearance of the reconstructed images, the maximum likelihood method outperforms the others from the point of view of estimating average activity in individual neurological structures of interest.

I. INTRODUCTION

In this article we concentrate on a method motivated by emission computerized tomography, which has as its major emphasis the quantitative determination of the moment-to-moment changes in the chemistry and flow physiology of injected or inhaled compounds labeled with radioactive atoms. In this case the function to be reconstructed is the distribution of radioactivity in a body cross-section and the measurements are used to estimate the total activity along lines of known location. One of the things that distinguishes this problem from that arising from X-ray computerized tomography is that the measurements tend to be much more noisy. For this reason, it appears desirable for an image reconstruction method which is to be used in emission tomography to incorporate an estimation procedure which depends on the statistical nature of the noise in the measurements.

Specifically, we concentrate on positron emission tomography (PET). In PET, the isotope used emits positrons, which within a few millimeters of their origins annihilate with nearby electrons, resulting in two photons travelling away from each other in (nearly) opposing directions. Near-simultaneous detection of these two photons approximately determines the line along which the emission has taken place. We count such coincidences for a number of lines over a period of time; the number of coincidences for a line is clearly related to the integral of the concentration of the radionuclide along the line. From such measurements we wish to estimate the distribution of the radionuclide at individual points in the cross-section. (In this discussion we have repeatedly idealized the physical situation, e.g., we have talked about cross-sections as if they were infinitesimally thin. The effect of such idealizations on the efficacy of the resulting algorithms is carefully treated in the literature [1]–[5]; in what follows we work with a mathematically idealized problem without any further justification.)

The emission of positrons is a Poisson process [2], the mean of which is determined by the concentration of the isotope. It is the latter that we wish to determine. More exactly, we are aiming at recovering a function whose value is the expected number of coincidences (generated photon-pairs) along a line per unit length during the data-collection period. (We are assuming, as is physically justified, that the activity is isotropic. Note also that the dimensionality of what we are reconstructing is "inverse length." ) The cross-section where the activity takes place can be enclosed by a square-shaped region. We discretize our problem by subdividing this square-shaped region into small abutting square-shaped picture elements (pixels, for short) and assuming that the activity in each pixel is constant. (This is a common approach to image reconstruction from projections [1]–[5]; for a discussion of what it might mean for the approach taken in this paper see [6], including the printed comments following it.) This approach is represented in Fig. 1 where $x_j$ denotes the ex-
expected number of coincidences per unit length in the vector whose 
use \( Y \) (1 pixel \( Y \)) the for the ith line during the data collection period and call \( (Y_i) \)

Fig. 1. The geometry of data collection for a single line. The expected
number of coincidences per unit length in the \( j \)th pixel is \( x_j \). The actual
number of coincidences counted for the ith line is \( y_i \). The length of inter­
section of the ith line with the jth pixel is \( l_{ij} \).

subject to \( x \in R^J_+ = \{x_j \geq 0, \text{for } 1 \leq j \leq J \} \). Such an
approach was proposed in [7] together with an iterative
algorithm for estimating the maximizer of (3). While
the algorithm was mathematically correct (the value of (3) was
monotonically increasing with the iterations), in its prac­
tical application to PET the iterations had to be stopped
before a deteriorating “checkerboard effect” (irregular
high amplitude patterns) showed up [6]. Thus maximizing
likelihood does not, at first sight, appear to be the approp­
riate optimization formulation for PET.

To overcome this difficulty, we previously proposed a
maximum a posteriori probability (MAP) maximization
approach [8]. We assumed a Gaussian prior probability
distribution for the image vector \( x \). (The Gaussian prior
had been previously used by us for CT [9] and has also
been investigated by others in the PET context; see, e.g.,
[10]. It is only one of a number of approaches that can be
used to overcome the difficulty; among others that have
been proposed we mention by the way of examples: MAP
with a Gibbs prior [11], the use of sieves [12], and early
stopping of a likelihood maximizing iterative process ac­
ccording to some statistical criterion [13]. We did not carry
out a careful examination of the relative efficacy of these
proposed methods for any particular medical task and so
we make no claims whatsoever as to the relative merits of
the methods proposed in this paper to the above-men­
tioned alternatives. It is, however, the case that the meth­
odology that we propose below for the evaluation of the
comparative efficacy of reconstruction algorithms can be
used by anyone wishing to demonstrate the statistically
significant superiority for a particular task of any one of
these methods over any other.) Combining the probability
density function of a Gaussian prior with (2) in Bayes’
formula for a posteriori probability, we replaced the
problem of finding an \( x \) in \( R^J_+ \) which maximizes (3) by
the problem of finding an \( x \) in \( R^J_+ \) which maximizes an
expression of the form

\[
\sum_{j=1}^{J} \left[ y_i \ln \left( \sum_{j=1}^{J} l_{ij} x_j \right) - \sum_{j=1}^{J} l_{ij} x_j \right] - \frac{\gamma}{2} \sum_{i, t=1}^{J} (x_i - m_{it})S_{it}(x_i - m_{it}). \tag{4}
\]

(Here we adopt the convention that the entries of the \( S \)
matrix are dimensionless and so \( \gamma \), which is always posi­tive,
has dimensionality “length squared.”) A legitimate
objection which can be raised to this approach is that a
Gaussian is not an appropriate prior since its probability
density function is not restricted to the domain \( R^J_+ \) of
the likelihood function. However, maximizing (4) makes
sense as it stands, even without a statistical justification,
since (as we shall see) the second term can be thought of
as a penalty function enforcing smoothness. Neverthe­
less, the applicability of the expectation-maximization
approach of [8] (on which the algorithm proposed below
An iterative algorithm for maximizing (4) was proposed in [8] for the special case when $S_{uv} = 0$ for $u \neq v$. It was demonstrated there that, for an appropriate choice of the $m$ vector (the prior expected value of the image vector) the “checkerboard effect” is prevented.

Nevertheless, it seems to us more desirable to have an $S$ matrix in (4) which enforces smoothness, rather than nearness to a prior mean. One possible choice for such an $S$ is defined as follows [2]. Let $N$ denote the set of indexes $j$ for which the $j$th pixel is not on the border of the picture region. Let, for $1 \leq j \leq J$, $N_j$ denote the set of indexes associated with those at most eight pixels which share a vertex with the $j$th pixel. Finally, let $S$ in (4) be the matrix such that

$$x^T S x = \sum_{j \in N} \left( x_j - \frac{1}{8} \sum_{k \in N_j} x_k \right)^2$$

and let $m$ in (4) be the zero vector. (Note that this is less restrictive than it appears at first sight. The functional in (5) would have the same value for any $m$ with constant components. Thus, our approach does not bias the reconstruction towards the zero vector, it simply biases it towards a smooth vector.) Choosing $S$ and $m$ in this way, we end up with a MAP approach to PET in which a likelihood maximization term is penalized by a term enforcing smoothness. The nature of the actual entries of the matrix $S$ is discussed below.

Having fixed $S$ using (5), the amount of smoothness that is enforced by maximizing (4) depends entirely on $\gamma$. The methodology of Section III below is applicable for finding the appropriate $\gamma$ for a particular task.

II. AN ITERATIVE ALGORITHM

We base our approach on [8]. Since, as will be made clear below, there is an essential additional assumption made in that paper, we first need to make a change of variables so that the results of [8] become applicable.

We define the $J \times J$ matrix $W$ by

$$W_{ij} = \sum_{i=1}^{J} l_{ij}$$

for $1 \leq j \leq J$ and $W_{uv} = 0$ if $u \neq v$. Since $W_{ij}$ is the sum of the lengths of the line segments in the $j$th pixel, it is a reasonable assumption that $W_{ij} \neq 0$ for any $j$ and so $W$ is invertible. We define, for $1 \leq i \leq I$ and $1 \leq j \leq J$,

$$\tilde{x}_j = W_{ji} x_j \quad \text{and} \quad a_{ij} = l_{ij}/W_{ij}.$$  

The physical interpretation is that $\tilde{x}_j$ is the expected value of the number of coincidences which originate in the $j$th pixel (a dimensionless quantity) and $a_{ij}$ is the probability that a coincidence which originates in the $j$th pixel will be detected along the $i$th line (see Fig. 1). Clearly, for $1 \leq j \leq J$,

$$\sum_{i=1}^{I} a_{ij} = 1$$

which is a property needed to apply the approach of [8]. Since, obviously,

$$\sum_{j=1}^{J} l_{ij} x_j = \sum_{j=1}^{J} a_{ij} \bar{x}_j$$

for $1 \leq i \leq I$, we can restate the optimization problem at the end of the last section as follows. Find the $J$-dimensional vector $\tilde{x}$ in $\mathbb{R}^J$ which maximizes

$$\sum_{j=1}^{J} \left( y_j \ln \left( \sum_{i=1}^{I} a_{ij} \bar{x}_j \right) - \bar{x}_j \right) - \frac{\gamma}{2} \sum_{u,v=1}^{J} \tilde{x}_u H_{uv} \tilde{x}_v$$

(10)

where $H = W^{-1} S W^{-1}$ and $S$ is the matrix of (5). From this we get the sought after vector by $x = W^{-1} \tilde{x}$.

Under the condition (8), it is proposed in [8] that starting with a vector $x^{(0)}$ with all components positive, the following iterative process will converge to an $\tilde{x}$ which maximizes (10). Given $x^{(k)}$ choose $x^{(k+1)}$ so that

$$-1 + \frac{x_j^{(k)}}{x_j^{(k+1)}} \sum_{i=1}^{I} a_{ij} x_i^{(k)} - \gamma \sum_{u=1}^{J} H_{ju} \tilde{x}_u^{(k+1)} = 0$$

(11)

is satisfied for $1 \leq j \leq J$.

The difficulty with solving (11) for a general matrix $H$ is that it is a coupled system of $J$ quadratic equations, and in our application area $J$ is typically of the order $10^4$ to $10^5$. This is why in [8] only the special case when $H$ is diagonal (and hence the equations are not coupled) is considered.

In the current paper we are dealing with a matrix $H = W^{-1} S W^{-1}$ where the $W$ are diagonal and $S$ is the smoothing matrix defined by (5). It is easy to show [2] that, for such an $H$, $H_{uu} = 0$ unless both $u \in N_j$ or $u \in N_j$ for some $v \in N_j$. (In other words, $H_{uu} = 0$ unless the pixel indexed by $u$ is in the $5 \times 5$ neighborhood of the pixel indexed by $j$. This becomes clearer below where we discuss the computation that is involved in multiplying a vector by the matrix $S$.)

A generalization of the method indicated by (11), described in the image reconstruction context in [14], can now be used to obtain an alternate sequence of $x^{(k)}$ converging to the required $\tilde{x}$. The difference is that in every iterative step we only choose every 9th pixel value to be changed (one in every 3rd row and in every 3rd column), keeping all other pixel values constant. Then, for each of the pixel values to be changed, $x_j^{(k+1)}$ can be calculated by solving a simple quadratic equation, since in (11) $x_u^{(k+1)} = x_u^{(k)}$ for those $u \neq j$ for which $H_{uu} = 0$.

By varying the subset of changing pixels we loop through all the pixels in 9 iterations. In any one iteration, the update is
independent of the other updates and is identical in its
dependence on the neighbor values for all pixels to be
updated. This indicates that parallel implementation is
appropriate. This scheme corresponds to a coloring of the
dependency graph of the underlying computations, which
is common in the parallel solution of differential equa­
tions [15]. Although the method updates during nine itera­

tions each pixel value exactly once, these nine iterations
are still much slower than one iteration with a
diagonal $H$. The reason for this is that much of the com­
putational work is in calculating inner products, such as
shown in (10), for the current estimate, and this has to be
repeated for each iteration.

The parallelism of the algorithm would be increased by
an order of magnitude if all $\tilde{x}_j$ were updated simulta­
aneously. This can be achieved by using the method de­
scribed above, updating all $\tilde{x}_j$ as if the other pixels in the
$5 \times 5$ neighborhood were not updated in the same step.
If this algorithm has the desired convergence properties,
$\gamma$ time it is likely to have a much superior computa­tional
performance.

To be precise, the iterative step of the proposed algo­
rithm is obtained by solving for $\tilde{x}_j^{(k+1)}$ the quadratic equa­tion

$$
\gamma H_{ii}(\tilde{x}_j^{(k+1)})^2 + \left(1 + \gamma \sum_{u \neq j} H_{ij}\tilde{x}_u^{(k)}\right)\tilde{x}_j^{(k+1)}
- \tilde{x}_j^{(k)} \frac{1}{\sum_{n=1}^{N} a_{jn}\tilde{x}_n^{(k)}} = 0.
$$

(12)

We note that we are really interested in $x = W^{-1}\tilde{x}$ and
not in $\tilde{x}$. If the $x^{(k)}$ converge to $\tilde{x}$, then the $x^{(k)} = W^{-1}\tilde{x}^{(k)}$
converge to $x$. Substituting into (12) we get the following
iterative relationship:

$$
\gamma S_{jj}(x_j^{(k+1)})^2 + \left(W_{ij} + \gamma \sum_{u \neq j} S_{ij}\tilde{x}_u^{(k)}\right)x_j^{(k+1)}
- x_j^{(k)} \frac{1}{\sum_{n=1}^{N} l_{jn}\tilde{x}_n^{(k)}} = 0.
$$

(13)

So by a roundabout route we have arrived at an iterative
algorithm for finding the $x$ which maximizes (4), for the
zero vector $m$.

There are two things worthy of note regarding the al­
gorithm. First, it is applicable to the problem with an arbi­
trary $S$ matrix (and indeed it is easily generalizable to a
nonzero $m$). Second, we do not have a convergence proof
for the algorithm. We got to it by looking at the algorithm
of [14] for the special $S$ matrix of (5) and by designing a
similar procedure which is likely to be faster. Prior to dis­
cussing the evidence available regarding the validity of
this algorithm, we give some general comments on the
implementation of the iterative step expressed in (13).

We rewrite this iterative step as follows. For $1 \leq j \leq J,$

$$
p_j = \frac{W_{ij}}{\gamma S_{jj}} - x_j^{(k)} + \frac{1}{S_{jj}} \sum_{u \neq j} S_{ij}\tilde{x}_u^{(k)}
$$

(14)

$$
q_j = \frac{x_j^{(k)}}{\gamma S_{jj}} \sum_{u \neq j} \frac{l_{ij}\tilde{x}_u^{(k)}}{\sum_{n=1}^{N} l_{jn}\tilde{x}_n^{(k)}}
$$

(15)

$$
x_j^{(k+1)} = \frac{1}{2} (-p_j + \sqrt{p_j^2 + 4q_j}).
$$

(16)

We take the $+$ sign in front of the square root in (16) to
insure the positivity of $x^{(k+1)}$.

Since $W_{ij}$ and $S_{ij}$ do not depend on the iteration number,
we calculate prior to starting the iterative process two
$J$-dimensional vectors whose $j$th components are $p_j$ and
$q_j$, respectively. (The definition of $S_{ij}$ follows from the
next paragraph.) In the iterative step we first calculate a
vector $p$ whose $j$th component is $p_j$, then a vector $q$ whose
$j$th component is $q_j$ and finally the vector $x^{(k+1)}$.

For the calculation of $p$, we observe that the only part
of the computation that is worthy of note is the application
of the matrix $S$ to the vector $x^{(k)}$. It has been proved [2]
that $S = KZK$ where the image $Kx$ can be obtained from
the image $x$ by convolving it with a $3 \times 3$ kernel with
central value $1$ and all other values $-1/8$, while the im­
age $Zx$ can be obtained from the image $x$ by setting $x_j$ to
zero for $j \notin N$. Thus, the computation of $p$ can be carried
out using standard image processing steps on $x^{(k)}$. (Note
that using this method, we do not need to calculate the
entries of the matrix $S$ explicitly. However, this can easily
be done. For example, for a row associated with an inter­
ior pixel, the entry associated with the pixel two above and
two to the left in the image is $1/64$.)

The efficient computation of $q$ depends on the fact that
$l_{ij}$ is nearly always zero (see Fig. 1). In our software for
image reconstruction from projections [16] there is a sub­
routine which for a specified line $i$ returns the list (of
length $T$ say) of those $n$ for which $l_{in} \neq 0$ together with
a list of the corresponding values of the $l_{in}$. This allows us
to calculate efficiently the inner product in the denom­
inator in (15). Using such a subroutine we build up a
$J$-dimensional vector $q$ as follows. We initialize $q$ to be
a zero vector and then apply the following computation in
which we refer by $n(t)$ to the $rth$ element of the list of
$n's$ and by $l(t)$ to the $rth$ element of the list of the corre­
sponding $l_{in}$ returned by our subroutine. Thus, $l(t) = l_{in(t)}$.

Begin ALGORITHM FIND-$\bar{q}$,
for $1 \leq i \leq I$
set $s_i = \sum_{t=1}^{T} l(t)x^{(k)}_{n(t)}$
for $1 \leq r \leq T$
set $q_{n(t)} = q_{n(t)} + l(t)y_i/s_i$
endfor,
end ALGORITHM FIND-$\bar{q}$.

When this is completed, we set, for $1 \leq j \leq J$, $q_j =
(x_j^{(k)} \cdot \bar{q})/(\gamma S_{jj})$. 

between the two algorithms is quite remarkable. One may think that this is due to the fact that $\gamma$ is so small (and therefore the method of smoothing does not matter), but it turns out that the match is even closer for $\gamma = 1$. In Table I, we report on the values of (4) at the 100th cycle for the two algorithms with $\gamma = 0.001$ and $\gamma = 1$.

As far as timings are concerned, the new algorithm of (14)-(16) is, as expected, much faster than the algorithm of [14]. For the case of $I = 16290$ and $J = 16129$ the execution times of the most optimized versions of the two algorithms (see [17]) for 25 cycles are 129.3 and 960.4 s, respectively.

This and the other experiments reported in [17] provide very strong evidence that the algorithm of (14)-(16) converges to the maximum of (4) for the useful range of $\gamma$'s and that, for this range, its behavior cycle-for-cycle is extremely similar to that of the algorithm of [14]. However, the computational cost of the new algorithm is nearly an order magnitude less.

### Table I

VALUES OF (4) FOR THE ALGORITHMS OF (14)-(16) AND [14] FOR $\gamma = 0.001$ AND $\gamma = 1$ AT THE 100th CYCLE FOR AN EXAMPLE WITH $I = 16290$ AND $J = 16129$

<table>
<thead>
<tr>
<th>$\gamma$</th>
<th>(14)-(16)</th>
<th>[14]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.001</td>
<td>7490224.64</td>
<td>7490222.18</td>
</tr>
<tr>
<td>1</td>
<td>7488599.58</td>
<td>7488599.47</td>
</tr>
</tbody>
</table>

By this implementational approach it is feasible to apply the algorithm to quite large problems ($I$ and $J$ greater than $10^4$) even on a SUN3 workstation. However, the size of our computational experiments (involving the reconstruction of a large number of images) brought us to investigate the possibility of a parallelized implementation, details of which are reported in [17].

Since we do not have a convergence theorem for our algorithm (14)-(16), we carried out a large number of tests to check its behavior under different circumstances. In [17] we report on some of these experiments. There we use the phrase "a cycle" to describe a period during which each pixel is updated exactly once. For the algorithm of (14)-(16) each iteration is a cycle, but for the algorithm of [14] nine iterations form a cycle. The computational cost of each iteration is approximately the same in the two methods, and so one cycle of [14] is approximately nine times more expensive than one cycle of (14)-(16). Here we present just one representative experiment.

In Fig. 2 we show our results for an experiment in which $I = 16290$, $J = 16129$, and $\gamma = 0.001$. The match between the two algorithms is quite remarkable. One may think that this is due to the fact that $\gamma$ is so small (and therefore the method of smoothing does not matter), but it turns out that the match is even closer for $\gamma = 1$.

### III. Performance Evaluation

Iterative image reconstruction methods have been with us for two decades now [18]. Their flexibility, which allows one to adapt them to particular tasks, is usually cited as the justification for choosing them. Nevertheless, they are not nearly as often used as the (noniterative) transform methods. The main reason for this is that the iterative methods tend to be computationally much more expensive [2]. Cost considerations also influence their efficacy for practical tasks: the experimental adjustment of free parameters in them (such as the number of iterations) so that they become optimal for the task at hand has been considered prohibitively expensive in the past.

The enormous decrease in the cost of computation in recent years substantially changes this situation. It is now feasible to experimentally optimize an iterative image reconstruction method for a specific medical task and to evaluate the relative efficacy of two reconstruction methods for a particular task in a manner which meets the high standards set by the methodology of statistical hypothesis testing [19]. The pioneering work in this direction is due to Hanson; see [20] and its references.

We illustrate our PET-oriented development of this approach by comparing the method of Section II to an expectation maximization (EM) method which maximizes likelihood (ML) [7]. We compare the efficacy of these two methods, for three different numbers of iterations, from the points of view of three tasks: detection of rela-
tively higher uptake on the left versus the right side of the brain; estimation of the total uptake in various neurolog­
cal structures; and estimation of uptake at individual points within neurological structures of interest. We also compare the performance of the six iterative techniques (two methods times three iteration numbers) with that of two variants of a transform method (the so-called con­volution or filtered-backprojection method).

In order to make our experiments realistic from the point of view of a clinical imaging task, we used a computer­ized overlay atlas based on average anatomy [21]. This atlas consists of 26 overlays each corresponding to a transaxial slice of the brain. Neuroanatomical structures are represented by ellipses and rectangles at appropriate locations; they are symmetrical with respect to the mid­line. We made use of this symmetry to set up our exper­iment as follows.

We created mathematical phantoms in which (in arbit­rary units) the activity in the brain background is 1.00 and in the neuroanatomical structures it is 1.95 or 2.00. For each pair of symmetric structures a random number generator chooses exactly one of the pair to have an activity of 2.00. The top-left image in Fig. 3 shows the 95 x 95 digitization of one such phantom. The same digitization (see Fig. 1) was used for all the reconstructions. Since we used 26 different overlays with several structures in each (there are 26 structures, in addition to the background shape, in the overlay shown in Fig. 3), it does not seem reasonable to provide here detailed descriptions of them. These data are available from the authors.

We generated images and projection data of these phan­toms using SNARK89 [16]. In generating the projection data we made an attempt to simulate the general charac­teristics of data that would be collected by a PET scanner. On the other hand, since our purpose is just to illu­minate our evaluation methodology, we did not attempt to sim­ulate any particular PET device. Therefore, our specific cri­teria about the relative merits of various methods may very well be incorrect when applied to a particular scanner. However, the same methodology becomes applicable to any scanner, provided that the data are generated to reflect the physical characteristics of that particular de­vice. Specifically, we think of our generated data as what one would use in the reconstruction algorithm; that is, data after corrections for effects such as attenuation have been made.

In our simulations we assumed a ring of 300 detectors with each detector in coincidence with 101 detectors op­posite it. (In SNARK89 terminology, we have a divergent ray geometry with 300 views and 101 rays/view. Be­cause of the X-ray CT, rather than PET, orientation of SNARK89, it was easier to use such an organization. Its consequence in PET terminology is that two separate measurements are made for each pair of PET detectors. The distance between the detectors was selected so that the fan of rays in a view cover the region of the brain in all phantoms and that the length of the side of a pixel is about the same as the distance between two rays at the center of the reconstruction region.) Using SNARK89 projection data are generated using line integrals over the original structures (rather than over digitized versions of them). Poisson noise was introduced into the measure­ments on the basis of a total of 3 000 000 coincidences collected per slice. Although this averages approximately 100 coincidences per SNARK89 ray (and so it may appear that the normal approximation to the Poisson distribution is justified), we note that for many rays the expected num­ber of coincidences will be much less. All the resulting ray sums were further deteriorated by 10% multiplicative Gaussian noise, to take care of other sources of error be­sides photon statistics. (Although this additional noise is statistically generated, it is thought of very differently from the Poisson noise due to photon statistics. It is in­troduced to simulate systematic, but to the user unknown, errors in the data after all corrections to the collected data have been made. Since the ray sums are by far the largest for the center of each projection, adding 10% multiplica­tive noise introduces a larger error near the center than elsewhere in the projections. Nevertheless, one can rea­sonably argue that even such additional noise does not adequately describe noise in real PET data after attenua­tion correction and scatter deconvolution. However, since our main purpose here is to illustrate our evaluation meth­odology, rather than to make a final decision regarding the superiority of any particular algorithm for any partic­ular PET instrument and for any particular medical task, we feel that including such additional noise to take care of the errors whose nature we cannot model statistically makes our illustration sufficiently realistic to demonstrate the usefulness of our evaluation approach. We also note that this additional noise is not modeled in the likelihood function. This reasonably reflects the real situation; there will always be some discrepancy between an actual PET instrument and a mathematical/statistical model of its be­havior.)
For our evaluation experiments 1000 phantoms and their projection data were generated: the overlay on which the phantom was based, the sides of elevated activity, and the noise in the data were independently randomly generated each time.

Preliminary experiments were done on an independently generated smaller set of phantoms and projection data (referred to as the training set) to find values of the free parameters for the reconstruction methods which are optimal for certain tasks performed on the training set [22]. Some of the details of how the choices were made are given below with the description of the tasks.

The methods that we compared were the convolution method (see, e.g., [2]) and two EM-type algorithms, one for maximizing likelihood (3), and the other is the method of (14)-(16) for MAP estimation (4). For the iterative methods, we used for the initial 0th iterate \( x(0) \) a uniformly grey image, in which the common grey value assigned to every pixel is the average grey value in the image as estimated from the measurement vector by the method of [2, p. 106]. (This value is automatically calculated by SNARK89 during the reading of the projection data.) We used the computer implementation described in [17]; in the case of ML this results in a pure EM algorithm without any “acceleration” or other tricks. Because of this, there were no free parameters to optimize in the ML case, except the iteration number. Based on the experiments in [22], we picked iteration numbers 2, 28, and 80 as worthy of further study. (A very reasonable question that can be raised is the following: since the different methodologies have been introduced with the justification that they optimize certain functionals, what is the point of even looking at the results of iterative procedures which have been terminated far short of convergence? Our answer to this is three-fold. First, preconvergence termination is a commonly made recommendation in our field; see [13], which is the most recent, at the time of writing, of a long series of publications discussing the practical appropriateness of early stopping. It seems to us worthwhile to evaluate what is after all common practice. Second, it can be shown for a large family of iterative reconstruction algorithms that truncating the iterative process provides an optimum according to a regularized version of the original functional [23], [24]. Under such circumstances, studying early iterates is similar to studying the optimization problem with varying weights of a smoothness constraint. There is a sound theoretical foundation to this approach of “regularizing by early stopping,” see [23], [24] and their references. In conjunction with a functional such as (4), the total smoothing is a combined effect of the choice of \( \gamma \) and the number of iterations. The methodology described here can be used to find the best combination of \( \gamma \) and iteration number for a particular task. Third, the cost of the reconstruction is proportional to the number of iterative steps. If the desired behavior, from the point of view of the medical task, can be achieved in fewer steps, then continuing with iterations is just a waste of resources. Such cost considerations should certainly enter into the combined choice of \( \gamma \) and iteration number. Since our data set does not correspond to any existing PET scanner, there is no point in finding such optimal combinations based on it. However, such work should be carried out by anyone wishing to optimize algorithms of this type for an actual scanner.)

For the convolution method we had to select a filter. Using the training set, we found that a very smoothing filter is the most appropriate for the detection task; it is one which sets all frequencies to be zero beyond eight-tenths of the Nyquist rate (in SNARK89 terms: cutoff = 0.8) and otherwise has the shape of the generalized Hamming filter with \( \alpha = 0.5 \) [2]. This is quite different from what has been found most useful for X-ray CT, which would typically be a generalized Hamming filter with \( \alpha = 0.8 \) and cutoff = 1.0 [2], [16]. Reconstructions using these two filters are shown in the middle and on the right, respectively, in the top row of Fig. 3.

For the MAP estimation we had to select the weight \( \gamma \) to be given to the smoothing prior in (4). Using the training set we found \( \gamma = 10 \) to be the most appropriate for the detection task and so we decided to do all our evaluations for only this specific value. (This implies that there may be much more appropriate values for the other tasks; this will have to be looked at prior to making any final recommendations regarding the relative merits of the methods.) The middle and the bottom rows of Fig. 3 show reconstructions by the EM algorithms, for ML and MAP, respectively, after 2, 28, and 80 iterations.

To evaluate the various reconstruction methods we made use of three medically reasonable figures of merit (FOM's).

1) Detection of Relatively Higher Uptake: Here we make use of the fact that structures in our phantoms form symmetric pairs. For each structure we define the abnormality index in the reconstruction to be the average of reconstructed pixel values for those pixels whose centers are within that structure in the phantom. A pair of symmetric structures provides us with a hit, if the abnormality index in the reconstruction is higher for that structure in the pair for which the activity is higher in the phantom. The FOM is the ratio of hits to the total number of pairs in the data set, and we refer to it as the hit-ratio. (One can reasonably hope that this mathematically defined hit-ratio would correlate with human performance in deciding the side of the relatively higher uptake. However, the actual value of the numerical hit-ratio is likely to be considerably higher than that of the corresponding measure for humans, since a human reader would not have knowledge of the exact location of the structures to be compared and would have greater difficulty in perceiving the relative sizes of the average uptake over structures.)

If we find that one method is more accurate than another one according to this FOM, then we are still faced with the problem of deciding whether or not our finding is statistically significant. We adopt the sign test [19] to provide us with a level of significance for rejecting the null-hypothesis that two reconstruction methods are...
equally good in favor of the hypothesis that the one with the greater hit-ratio is better.

In this approach to statistical significance, we look only at those pairs of structures which have been classified differently by the two reconstruction methods. Let $C$ be the total number of such pairs. Let $c$ be the number of pairs that have been correctly classified by the reconstruction method with the higher hit-ratio. The null-hypothesis that the methods perform equally well implies that $c$ is a random sample from a binomial distribution with total number of items $C$ and equal probabilities assigned to the two classes. We can now use this binomial distribution to see what is the probability of randomly selecting an element from it with value $c$ or higher. This probability provides us with our level of significance for rejecting the null-hypothesis.

The choices for the free parameters in the convolution method and for $\gamma$ in (4) were made in [22] so as to optimize the algorithms from the point of view of the hit-ratio. In Fig. 4, we plot the average values (over 78 phantoms from the training set) of the hit-ratio. It is based on this plot that we selected iteration 2 as worthy of further study.

2) Estimation of Total Uptake in Neurological Structures: For each neurological structure, we define the inaccuracy to be the absolute value of the difference between the abnormality indexes of that structure in the reconstruction and in the phantom. We define the structural accuracy to be the FOM which is the negative of the average of the inaccuracy over all structures in all phantoms.

The level of statistical significance for rejecting the null-hypothesis that two reconstruction methods are equally good in favor of the hypothesis that the one with higher structural accuracy is better is calculated as follows. Let $\beta_b$ and $\delta_b$ be the inaccuracies of the $b$th of altogether $B$ structures as reconstructed by the two methods, respectively. Then, according to the null-hypothesis, $\beta_b - \delta_b$ is a sample of a zero-mean random variable. It follows, for large enough $B$, that

$$\sum_{b=1}^{B} (\beta_b - \delta_b)$$

is a sample of a normally distributed zero-mean random variable [19]. The variance of this random variable is $B$ times that of the zero-mean random variable of which the $\beta_b - \delta_b$ are samples for $1 \leq b \leq B$. Hence, for large enough $B$, it is reasonable to assume that the null-hypothesis implies that (17) is a sample from normally distributed random variable with mean zero and variance

$$\sum_{b=1}^{B} (\beta_b - \delta_b)^2.$$  

We can thus use the normal distribution to calculate significance [19].

3) Estimation of Pointwise Uptake in Neurological Structures: For this we used the so-called clipped normalized distance provided by SNARK89 [16]. Briefly, both the phantom and the reconstruction are clipped by setting pixel values which are less than (in our case) 1.65 to 1.65 and pixel values which are more than (in our case) 2.05 to 2.05. After this a normalized root square distance between the clipped reconstruction and clipped phantom is calculated. The clipping ensures that only the inaccuracy in and around neuroanatomical structures contributes to the distance measure. (Inside the neuroanatomical structures the values are either 1.95 or 2.0. However, the surrounding tissues have value 1.0. That means that after digitization, which involves taking averages over pixels, the edge pixels will have values less than 1.95. For some of the smaller structures, practically all the pixels are edge pixels. This is why we decided to place the clipping interval unsymmetrically at 1.65-2.05.) The FOM is the average of the negative of the clipped normalized distance over all the phantoms. We call this FOM the pointwise accuracy, since squaring of differences at individual pixels insures that large errors at just a few points will degrade the FOM.

Statistical significance is calculated in the same way as for structural accuracy, except that now we compare clipped normalized distances for whole phantoms (rather than inaccuracies for individual structures).

In Fig. 5 we plot the clipped normalized distances for five different phantoms in the training set both for ML-EM and for MAP-EM with $\gamma = 10$. It is the stability of the MAP approach from the point of view of such distance measures that motivated its study in the first place. In Fig. 6 we plot the average values (over 78 phantoms of the training set) of the clipped normalized distance. For ML-EM this average is minimum at iteration 28, which is why we selected iteration 28 as worthy of further study. The average monotonically decreases for MAP-EM. Based on Figs. 4 and 6, we considered that the performance of MAP-EM does not change significantly after cycle 80.

Table II reports on the rank-orderings of the eight reconstruction methods according to the three FOM’s. All differences between two successive methods in the ordering are statistically significant at the 0.001 level [19], unless otherwise indicated. If significance is not at the 0.001 level but is at the 0.01 level, that is indicated by a single minus sign after the rank of the reconstruction with the
Fig. 5. Clipped normalized distances for five phantoms in the training set reconstructed by ML-EM (first plot) and MAP-EM (second plot).

Fig. 6. The average over 78 phantoms of the training set of the clipped normalized distances. The convolution method indicated is the "smooth" one, which was chosen as being optimal for hit ratio. It is also preferable to the "rough" convolution method for this task (see Table II).

Using the notion of rank-ordering similarity [25] we can quantitate the differences in rank-orderings. This measure assigns the value 0 if the two rank-orderings to be compared are the reverse of one another, the value 1 if they are the same, and has the expected value of 0.34 for two randomly selected rank-orderings of length eight. The rank-ordering similarity of hit-ratio versus structural accuracy is 0.06, of hit-ratio versus pointwise accuracy is 0.25, and of structural accuracy versus pointwise accuracy is 0.49. So, for the first two cases the correspondence between the two rank-orderings is worse than random, and it is not much better than random even in the third case. These results warn us that one has to be very careful and not generalize from performance on one task to performance on another: the relative merits of methods and the optimal choices of the free parameters are extremely task-dependent. For an interesting theoretical discussion of the relations between FOM's provided by estimation tasks and classification tasks, see [26].

IV. DISCUSSION

We have presented a new iterate algorithm appropriate for image reconstruction from noisy data. It is designed to find an image which maximizes \textit{a posteriori} probability. The actual function to be maximized consists of a maximum likelihood term (based on the Poisson statistics of the data collection) penalized by a term which is designed to enforce local smoothness. Although we do not have a convergence proof for the algorithm, we have demonstrated that it appears to produce the same value for the function to be maximized as a previously proposed (slower) algorithm for maximizing the same objective.

TABLE II

<table>
<thead>
<tr>
<th>Method</th>
<th>Parameter</th>
<th>Hit-ratio</th>
<th>Structural Accuracy</th>
<th>Pointwise Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ML-EM</td>
<td>2</td>
<td>1 - - -</td>
<td>7</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>7 - -</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>MAP-EM</td>
<td>2</td>
<td>2</td>
<td>8</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>convolution</td>
<td>smooth</td>
<td>5 - - -</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>rough</td>
<td>8</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

higher FOM. Similarly, double minus sign indicates significance only at the 0.05 level, and triple minus sign indicates that difference is not significant at the 0.05 level. We note that in all cases the difference between a method and another which is ranked two below it was significant at least at the 0.05 level.

The main conclusion to be drawn from this table is the extreme dependence of the relative merit of two reconstruction methods on the task to be performed. The second iterate of ML-EM was the best for detecting relatively higher uptake, but it had the worst pointwise accuracy and the second worst structural accuracy. The eightieth iterate of ML-EM was the best for estimating average uptake within structures, but it was the second worst for detecting relatively higher uptake and the third worst for pointwise accuracy. The eightieth iterate of MAP-EM was the best for pointwise accuracy within the neurological structures, nevertheless it was the third worst for detecting relatively higher uptake. The worst for detecting relatively higher uptake was the convolution method with the rougher filter, but it was the second best for estimating average uptake within the structures.
function. An efficient parallel implementation is reported elsewhere [17]. The efficiency of our implementation means that experiments that we need to carry out (for example for finding the optimal \( \gamma \) for a particular medical problem involving positron emission tomography) can be done in an acceptable period of time even though they involve reconstructing a large number of images. This allows us to adjust our reconstruction algorithm to particular medical needs. It also allowed us to compare our new algorithm with ML-EM and the convolution method, to obtain some rather interesting results and to show that these results have a high level of statistical significance. We summarize these results as follows.

First, (the eightieth iterate of) our method outperformed all others that we tried from the point of view of pointwise accuracy. We must note, however, that the free parameters in the MAP and convolution methods were not selected to optimize this particular FOM, and so the results may well turn out to be different for the optimal choices of the free parameters.

Second, in spite of its relatively large pointwise accuracy, our method is outperformed by both ML-EM and the “rough” convolution method from the point of view of structural accuracy. Although the comment regarding the choice of free parameters applies here as well, this result is nevertheless of great interest as it stands. The reason is that we [8], as well as many others (e.g., [12–14]), invested a great deal of effort to overcome the perceived deterioration of images produced by the ML-EM algorithm, as demonstrated in Figs. 3, 5, and 6. However, from the point of view of the clinically-used FOM of structural accuracy [21], this deterioration is illusory; the “noise” in the reconstruction averages over the neurological structures of interest, providing us with good structural accuracy in spite of bad pointwise accuracy.

Third, our results on the hit-ratio are also very interesting. What these results imply is that for the detection of relatively higher uptake neither the ML nor the MAP maximization criterion is relevant, since the second iterate of the algorithms (which is optimal according to the hit-ratio) produces pictures with low likelihood (3) and low \( a \) posteriori probability (4). It is fortuitous that early iterates of the EM algorithms outperform the task-optimized convolution method from this point of view (see Fig. 4), but that has nothing to do with the reasoning behind the EM algorithms.

In conclusion, the method proposed in Section II seems to have great promise if pointwise accuracy in positron emission tomographs is desired. On the other hand, it does not offer an improvement over previously proposed methods for PET reconstruction from the points of view of structural accuracy or the detection of relatively higher uptake. These conclusions are based on simulated data (which do not exactly correspond to any particular PET scanner) and so may not carry over to specific scanners. However, more important than any of the specific conclusions is that we have demonstrated a statistically rigorous way of validating claims regarding the superiority of one image reconstruction algorithm over another for a specific task and have illustrated that the relative merit of two reconstruction algorithms can be extremely dependent on the intended medical task.

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