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## Iterative reconstruction algorithms in nuclear medicine

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### Abstract

Iterative reconstruction algorithms produce accurate images without streak artifacts as in filtered backprojection. They allow improved incorporation of important corrections for image degrading effects, such as attenuation, scatter and depth-dependent resolution. Only some corrections, which are important for accurate reconstruction in positron emission tomography and single photon emission computed tomography, can be applied to the data before filtered backprojection. The main limitation for introducing iterative algorithms in nuclear medicine has been computation time, which is much longer for iterative techniques than for filtered backprojection. Modern algorithms make use of acceleration techniques to speed up the reconstruction. These acceleration techniques and the development in computer processors have introduced iterative reconstruction in daily nuclear medicine routine. We give an overview of the most important iterative techniques and discuss the different corrections that can be incorporated to improve the image quality. © 2001 Elsevier Science Ltd. All rights reserved.

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### 1. Introduction

The goal of Emission Computed Tomography is to obtain an accurate image of theradioactivity distribution throughout the patient to extract physiological and pathophysiological information. In Single Photon Emission Computed Tomography (SPECT) the gamma camera rotates around the patient. By using mechanical collimation, which only allows nearly perpendicular incident photons, the camera takes planar images of the activity distribution in the patient. These planar images can be regarded as projection images of the activity distribution, and are reconstructed with different reconstruction algorithms. In Positron Emission Tomography (PET) [1,2] the 180° opposed photons, originating from a positron annihilation, are registered by electronic coincidence circuits. Such a measurement is called a Line-of-Response (LOR). The raw data set in PET is three-dimensional (3D) because together with in-plane LORs, oblique LORs which cross different planes are also accepted. These LORs are close approximations to line integrals, which adequately sample the activity distribution. By rebinning

the data to a 2D data set [3,4], the same reconstruction algorithms [5] as in SPECT can be used. If this is not done, the image reconstruction becomes more complex since the 3D object cannot be regarded as a set of independent slices anymore. A detailed description of the 3D reconstruction problem is given in Refs. [6–13]. For simplicity of notation, we limit this formulas for iterative reconstruction to 2D cases.

The standard reconstruction algorithm, to calculate the radioactivity distribution from the projections, is the Filtered BackProjection (FBP) technique, which is based on direct inversion of the Radon transform [14]. This inversion is derived for continuous sampling and then discretized for sampled data. The limited number of projection sets introduces streak artifacts [15] in the image reconstructions. Prefiltering is performed by a ramp filter, which is a filter proportional to the frequency and with zero value at the DC component. The purpose of this ramp filter is to remove blurring from the backprojection step, but the high-frequency noise of SPECT and PET images are amplified by this filter which results in noisy reconstructions. This effect can be limited by combining the ramp filter with a low pass filter. Despite its disadvantages, FBP is used extensively in nuclear medicine due to its short reconstruction times.

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## 2. Iterative reconstruction algorithms

Iterative reconstruction methods incorporate the discreteness of the data from the beginning. The true tracer distribution  $f(x, y)$ , which is discretized as an image of  $L \times L$  pixels, is represented by a vector  $\lambda(b)$  ( $b = 1, \dots, B$ ,  $B = L \times L$ ). If we have projections from  $N$  angles and  $M$  samples per projection, the acquisition data can be represented by a 1D vector of measurements  $n^*(d)$  ( $d = 1, \dots, D$ ,  $D = N \times M$ ). The vectors are related to each other by the following relationship:

$$n^*(d) = \sum_{b=1}^B p(b, d)\lambda(b) \quad (1)$$

with  $p(b, d)$  the probability of detecting a photon, originating in voxel  $b$ , in detection bin  $d$ . These probabilities form a  $B \times D$  matrix, which is often called the projection matrix. This is a set of linear equations which can be solved for  $\lambda(b)$ , if the probabilities  $p(b, d)$  and the measured data  $n^*(d)$  are given.

The inversion of this set of linear equations is difficult because of the large dimensions of the projection matrix (typical in SPECT  $B \times D = (128)^2 \times (128 \times 60)$ ). For direct inversion [16,17] the matrix should be available, but it takes a lot of memory to store its elements. Moreover, the direct inversion of such large matrices often results in severe problems due to numerical instabilities. This makes direct inversion very difficult to implement. Direct inversion methods are also relatively slow, which has led to the usage of iterative techniques. An initial estimate  $\lambda_0(b)$  of the radioactivity distribution is chosen and the algorithm tries to improve this estimation at each iteration. From an intermediate estimation  $\lambda^k(b)$  of the distribution, the forward projection  $n^k(d)$  is calculated. This calculation is compared with the measured projection  $n^*(d)$ . From this comparison correction terms are derived by backprojection, which are used to update the previous estimate  $\lambda^k(b)$  to  $\lambda^{k+1}(b)$ . By updating the previous estimate, the  $n^{k+1}(d)$  becomes more consistent with  $n^*(d)$  than the previous estimate.

All iterative reconstruction algorithms use this method to go towards the solution, but they differ from each other in the way the correction terms are derived and how the update to the new estimate is calculated. We will discuss the different classes of iterative algorithms in Section 2.1 and describe the best-known iterative algorithm in Section 2.2.

### 2.1. Classes of iterative algorithms

Iterative algorithms can be classified into two classes. The first class contains the conventional iterative algebraic methods, which reconstruct the images by solving the aforementioned set of linear equations (1). Examples are the Algebraic Reconstruction Technique (ART) [18,19], the Simultaneous Iterative Reconstruction Technique (SIRT) [6] and the Iterative Least-Squares Technique (ILST) [20].

The second class contains the iterative statistical recon-

struction methods, which reconstruct images by iteratively maximizing a likelihood function. They take the noise on the measurement data into account. Therefore they use a statistical modeling of the measurement process. The best-known example is the ML-EM algorithm. The projection data are Poisson variables with a mean equal to the line integral, perpendicular to the projection bin, through the activity distribution. For a large number of photons, the measured data is relatively close to the value of the line integral. For low count statistics, the measured data can have a large deviation of the mean. This is the reason why analytical algorithms (e.g. FBP), which assume the measured data are equal to the line integral, perform quite good in the case of high photon statistics, but bad for low count acquisitions. The Maximum Likelihood Expectation Maximization (ML-EM) [21,22] algorithm, which is described in Section 2.2, takes the Poisson nature of the data into account.

The statistical algorithms [23,24] can be further subdivided into one group which does not use a priori information, and a second group which takes into account a priori information [25,26]. This is useful to constrain the number of possible solutions to the ones which are acceptable. The positivity constraint is the best known. It ensures that all pixels have a non-negative value, which is reasonable because they should represent activity distribution. This is not guaranteed by FBP. There are more sophisticated priors as Median Root Prior [27,28], mostly used to guarantee good noise reduction and edge preservation.

Another advantage of the iterative methods is the possibility to incorporate image degrading effects into the projection matrix  $p(b, d)$ . Scatter, attenuation, depth-dependent resolution and geometrical weighting can be incorporated into  $p(b, d)$ . Including these effects results in a quantitatively improved reconstruction image. An overview of these correction possibilities is given in Section 4.

### 2.2. Incorporation of Poisson statistics

Shepp and Vardi [21,22] incorporated the Poisson nature of the acquired data in their reconstruction algorithm. If  $\lambda(b)$  is the true trace distribution in pixel  $b$ , the measurements  $n^*(d)$  are Poisson variables with mean equal to

$$\lambda^*(d) = \sum_{b=1}^B p(b, d)\lambda(b) \quad (2)$$

The goal of the reconstruction algorithm is to find the distribution  $\lambda(b)$  which has the highest probability to have generated the measured projection data  $n^*(d)$ . The probability function is called the likelihood function and is derived from the Poisson statistics

$$L(\lambda) = \prod_{d=1}^D e^{-\lambda^*(d)} \frac{\lambda^*(d)^{n^*(d)}}{n^*(d)!} \quad (3)$$

To maximize this likelihood Shepp and Vardi used the EM

algorithm, which yields the following update towards a new estimation:

$$\lambda_{k+1}(b) = \lambda_k(b) \frac{\sum_{d=1}^D p(b, d) n^*(d)}{\sum_{b'=1}^B p(b', d) \lambda_k(b')} \quad (4)$$

Taking the Poisson nature of the data into account improves the reconstructions compared to analytical algorithms, especially for low count data. On the other hand, it also introduces noise deterioration for a high number of iterations [29], which will be discussed in the next section.

### 3. Disadvantages of iterative reconstruction algorithms

#### 3.1. Noise deterioration

Initially the ML-EM algorithm converges towards an acceptable reconstruction. For higher iteration numbers, the likelihood still increases but the reconstructions get more noisy. The reason for this effect are the measurements which are Poisson random variables. A reconstruction with projection data which are very similar to the noisy measurement data, will be very noisy because the projector acts as a smoothing operator. Different techniques for solving this problem have been investigated. One possible way is to limit the possible reconstructions to the ones which are smooth enough. This can be done by requiring the image to be composed of sieves (Gaussian kernels) [29]. A second solution is to perform many iterations and postfilter the reconstruction. A third way is stopping the reconstruction, based on a stopping rule, before noise deterioration degrades the image quality of the reconstruction [30–32]. For clinical use, mostly the postfiltering method is used because the smoothness of the reconstruction can be chosen by using another cut-off frequency of the filter, without repeating the reconstruction process.

#### 3.2. Calculation time

The ML-EM algorithm has proven to be effective, but also to be too slow for daily routine. The time needed for a FBP reconstruction (backprojection of the whole data set) is approximately half the time needed for one iteration (one forward projection of the estimate and one backprojection of the whole data set) of the ML-EM algorithm. Depending on the settings of the algorithm and the desired convergence, 10–100 iterations are used for one reconstruction. Several methods have been proposed to speed up the algorithm [33–36], but none of these made the algorithm accepted in a clinical environment. Splitting up the measured dataset into different subsets and using only one subset for each iteration speeds up the algorithm with a factor equal to the number of subsets. This method was introduced by Hudson and Larkin in 1994. Since its introduction, the Ordered Subsets Expectation Maximization (OS-EM) [37] has

become the most frequently used iterative reconstruction algorithm in both SPECT and PET. In ML-EM every iteration requires a forward projection of the previous estimation into all projections (equal to the number of measured projections). In OS-EM the projection data are divided into ordered subsets. Each subset contains an equal number of projections. As an example, if a SPECT acquisition contains projections from 60 angles, one step of the ML-EM algorithm requires forward projections under 60 angles. In OS-EM data can be split up in e.g. 6 subsets of 10 angles, so one iteration step only requires forward projections under 10 different angles. Hudson and Larkin have shown that the image quality for the same number of iterations in ML-EM and OS-EM is comparable if the number of subsets is not too high. This means that for this particular case using OS-EM instead of ML-EM results in a speed up factor of 6. Further optimization of the speed is achieved by speeding up the forward and back projection [38–43].

### 4. Advantages of iterative reconstruction algorithms

#### 4.1. Improved modeling of the measurement process

In analytical algorithms such as FBP it is assumed that the measured data are line integrals through the activity object. Because of the aforementioned Poisson nature of the data and image degrading effects, such as attenuation and scatter, this assumption is not satisfied. The advantage of the discrete approach for iterative algorithms is that the entire acquisition process, including the interaction of the photons with the body, the collimator and the detector, can be incorporated directly in the  $p(b, d)$ . This is very complicated and therefore different approximations have been proposed to reduce the calculation time. Because the incorporation of these image-degrading effects is different in SPECT and PET, they will be discussed separately.

#### 4.2. Modeling of the image degrading effects in PET

In PET every LOR has an attenuation coefficient which is equal to the total attenuation along this LOR. These attenuation coefficients can be easily determined by performing a transmission scan of the patient, with either external positron emitters or single photon emitters [44]. Correction is easily done, prior to reconstruction, by dividing the emission data with the measured attenuation coefficients.

Also Point Spread Function (PSF) recovery is relatively easy in PET: the approximation of a position-independent PSF is quite accurate. The resolution recovery is done by replacing the projector with a two-stage operator: first the forward projection is calculated, and in a second step the projections are smoothed with a convolution mask, approximating the PSF. The backprojector, which is the adjoint of the projector, is replaced by a smoothing with the convolution mask followed by the backprojection. In the case of nuclear medicine imaging, the adjoint of the projector

reduces to the transposed of the projector since the projection operator is a real operator. The PSF is mostly approximated with a Gaussian kernel with width equal to the FWHM of the system.

Scatter correction is more difficult to include in the reconstruction [45]. Accurate forward modeling of the scattering needs intensive computations. The most accurate approach is Monte Carlo simulation, which generates every photon and follows its path through the body, collimator and detector. Along its path, the probability of photon–electron interaction is calculated. A random generator decides whether or not this interaction will occur for a photon. To use this in reconstruction, this process should be simulated for every patient as the interaction is body-dependent, which is practically impossible due to the long calculation times. To reduce processing times, different approaches have been published with an analytical approach for the scatter PSF. Empirical curves have been used to achieve a good fit to the measured data [46]. Others start from a physical model which is simplified by different approximations [47].

LORs at larger distance from the center of rotation have a lower detection probability. If no correction would be applied for this, the reconstruction of a uniform object would have lower activity towards the edge of the FOV. The probability for detection of the LOR can be derived analytically [48–50]. During reconstruction every forward projected LOR through the activity object can be weighted by dividing the forward projected value by the detection probability. This will result in uniform reconstructions. This method gives less noisy reconstructions than multiplying the final reconstruction with the inverse of the sensitivity [51]. This geometrical weighting is more important in dual or triple gamma camera PET than in full-ring PET [52].

#### 4.3. Modeling of the image degrading effects in SPECT

Due to their depth dependency, attenuation and resolution correction are more difficult to include in iterative reconstruction for SPECT. There is a lot of interest in the iterative methods with non-uniform attenuation correction for SPECT, since there is no analytical method to solve this effect exactly. To perform non-uniform attenuation correction, a map of attenuation coefficients should be available. This can be made from a Computed Tomography (CT) map by conversion of the attenuation coefficients to the energy of the  $\gamma$ -rays of the used radionuclide. The attenuation coefficients  $\mu(b)$  can be measured by equipping the gamma camera with transmission sources. First a blank scan  $b(d)$ , with no attenuating medium in the FOV, is measured. Afterwards the attenuating object is placed in the FOV and the same measurement is repeated. This is the transmission measurement  $t(d)$ . The relation with the attenuation coefficients is given by:

$$t(d) = b(d) e^{-\int_L \mu(x) dx} \quad (5)$$

with  $L$  the path from transmission source to detector. This is converted into the Radon transform of the attenuation map by:

$$t^*(d) = \ln \frac{b(d)}{t(d)} \quad (6)$$

which can be reconstructed by standard filtered backprojection or by using iterative methods. The ML-EM has been used with good results for this reconstruction [53], although the  $t^*(d)$  are no longer Poisson distributed. Once these attenuation coefficients are reconstructed, they can be used in the reconstruction of the emission data. In the forward projection, every pixel should be weighted by the attenuation factor determined by the attenuation map and the distance to the detector. Therefore each probability  $p(b, d)$  of detecting a photon, originating in voxel  $b$ , in detection bin  $d$  is multiplied by an attenuation factor  $w_A(b, d)$

$$w_A(b, d) = e^{-\int_{b \rightarrow d} \mu(x) dx} \quad (7)$$

with  $b \rightarrow d$  the path from pixel  $b$  to detector  $d$ . In the backprojection the transposed operation (attenuated backprojection) needs to be done.

In SPECT the resolution degrades with increasing distance from the detector. This depth-dependent blurring, caused by the collimator acceptance angle, has to be modeled and included in the projection. One way to model this is to replace one ray by a bundle of rays (forming an inverse cone) with origin in the projection bin. This technique is called ray-tracing. The second (more time-consuming) method is to rotate [54] the reconstruction matrix to a matrix parallel with the projection bins and to apply a distance dependent filter. This can be done by convolution in the spatial domain or by multiplication in the frequency domain. The third method (rotation and diffusion) is a more efficient implementation of the second method [55]. The reconstruction matrix is also rotated parallel to the projection bins, afterwards the following steps are done. The farthest layer is convolved with a small kernel, this is added to the second farthest layer. This sum is convolved with another small kernel, this is added to the next layer. This is repeated until the last layer is reached. This method is faster because the small kernel convolution is more efficient than the Fast Fourier Transform (FFT) with multiplication of the second method. The calculation of these small kernels from the depth-dependent PSF can be found in Ref. [55].

Scatter correction can be included in iterative reconstruction in the same way as described in Section 4.2. In SPECT however, scatter correction is mostly done by subtraction-based methods [56]. Before reconstruction, the scatter is estimated from the ratio of two or three energy windows this is subtracted from the window around the photopeak. This method is more accurate for SPECT than for PET because the energy resolution is better. The transmission-dependent convolution subtraction technique [57,58] can

estimate the scatter function iteratively if an attenuation map is available. This method is based on the convolution-subtraction method [59]. In this method the scatter is assumed to be a convolution of the invariant scatter function with the measured projections. This estimate is subtracted from the measured projection data. Because the invariant scatter function is only an approximation, this results in artifacts in high-contrast projection data. This method can also be implemented in the Fourier domain. The transmission-dependent convolution-subtraction technique uses the transmission map to define the inhomogeneous scattering object. The scatter fractions are estimated for all positions by using a regression equation. The scatter distribution is estimated by convolution of the projections with the scatter function. The scatter fraction of the total events is then determined for each projection bin by using the narrow-beam transmission values [56]. These spatially varying scatter functions are used to correct the projection data.

## 5. Conclusions

The difference between the different classes of iterative reconstruction techniques, which are used in PET and SPECT, was described. The main disadvantage (long reconstruction times) of iterative reconstruction has been minimized by the recent developments in processors and optimization of the algorithms. This allowed its introduction into nuclear medicine: first it was used for PET reconstruction, where the correction for attenuation and PSF are more easy to include than in SPECT. Further developments in iterative reconstruction will include the further development of simultaneous attenuation and emission map reconstruction [60] and better and faster scatter correction techniques [61,62].

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