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An investigation of accuracy of iterative reconstructions in quantitative SPECT

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Abstract. The iterative methods of image reconstructions represent the promising way for recovering the activity distribution from nuclear medicine acquisitions. One of the clinical areas where the accurate estimation of activity is extremely important is the radiotherapy of tumours. The goal of this study is to estimate the accuracy of the currently used in clinics iterative maximum likelihood expectation maximization (MLEM) methods in different realistic oncology situations. Numerical model was created to reproduce some of the clinical cases from the Internal Radiotherapy (IRT). Monte-Carlo simulations were utilized to generate sets of projections with the realistic noise level. The quantitative capability of the method was evaluated by performing a comparative analysis of true and reconstructed distributions. The influence of incorporation of physical effects (attenuation, scatter, and resolution loss) and algorithmic parameters (number of projections and iterations) on the solution accuracy and the convergence behaviour was studied.

1. Introduction

There is a well recognized clinical demand for imaging procedures that would provide quantitative information about the processes inside living organisms. In nuclear medicine (single photon emission computed tomography (SPECT), in particular) tracer molecules labeled with a radioactive isotope are injected into the patient body, and radioactive emissions from this isotope are recorded at several locations around the patient. The consequent diagnosis or therapy is based on the analysis of an image which is reconstructed from these data (projections).

In oncology application of SPECT, the assessment of the radiation dose and its distribution in tumors and critical tissues is of particular importance. Accurate determination of tracer distribution among tumors will lead to estimating of efficient patient-specific dose administered for cancer treatment. But this optimal internal radiotherapy (IRT) should be based on the accurate reconstruction of activity distribution from acquired SPECT projection data.

To provide clinicians with this quantitative information, a complex inverse problem needs to be solved with a maximum possible accuracy. In current SPECT systems, both 2D projections and 3D images have discrete character and represent values averaged over relatively small pixels or voxels. This converts the continuous inverse imaging problem into the system of algebraic equations:

\[ CX = Y \] (1)
where \( X = \{ X_i \}_{i=1,n} \) is the unknown vector of activity distribution, \( Y = \{ Y_j \}_{j=1,m} \) - the vector of measured data, and \( C = \{ C_{ij} \}_{i=1,n, j=1,m} \) is the system matrix. The elements of system matrix \( C_{ij} \) represent the probability that the photon emitted from the voxel \( i \) is detected in pixel \( j \).

For dosimetry applications, this system of algebraic equations (1) has the following features:

- large dimension of the matrix;
- under-determined (often) system \((m<n);\)
- noisy character of vector \( Y \).

One of principal conditions which needs to be fulfilled in order to obtain an accurate solution to this problem is that the coefficients of the system matrix are close to the true values. That means that model (1) properly reflects the ways in which the emitted photons are interacting with the body and are recorded by the detector. In order to do that, the elements of the system matrix should take into account a number of physical effects occurring during data acquisition. In the case of SPECT these include: (i) photon attenuation, (ii) scatter, (iii) collimator septal penetration (if applicable), and (iv) distance-dependent resolution loss.

These effects can be modeled and (with different level of accuracy) incorporated into the reconstruction procedure [3]. However, even after performing all these corrections, the complete activity recovery cannot be achieved due to limited spatial resolution of the imaging systems [4-5]. Potentially, an accurate compensation [5-8] for this limited spatial resolution can be made assuming that the shape of the studied object is known from other modalities (CT or MRI) and the activity distribution inside this object is uniform. However, for oncology applications, conventional hybrid SPECT-CT modalities don’t always visualize the boundaries of the tumors (using usual CT) or provide only approximate boundary information. In addition to an accurate estimation of the total activity within tumor, some oncology applications require the information about this activity distribution. Especially, for relatively large objects, knowledge about this distribution may be essential when creating precise treatment plans.

A number of studies [7-12] were devoted to investigating quantitative accuracy of SPECT reconstructions, potentially oriented to oncology applications. Monte Carlo simulations were utilized to validate reconstruction methods because activity distributions inside numeric phantoms are known. In most of these studies, only the total activity reconstructed inside the object was compared with the truth. In particular, in [7, 10, 11], the dependence of this parameter on the number of iterations was studied for objects having different sizes and shapes. In [9], the accuracy of volume estimation was analyzed. While in [12], a comparative analysis for both total activity and its distribution was performed for \(^{131}I\), that work was focused on validating different scatter correction strategies.

In our work, we investigate the accuracy of estimation of two quantitative parameters which are crucially important for \(^{99m}Tc\) SPECT-based dosimetry studies: total activity inside the object and the activity distribution. We tried to model in our studies the conditions which are usually encountered in a clinical environment, therefore, the reconstructions were performed using the iterative maximum likelihood expectation maximization (MLEM) method that is currently used in clinics. In order to reproduce in our investigations the variety of clinical versions of the MLEM algorithm, we first applied simple versions of the MLEM method with only partial corrections for the aforementioned physical processes. Then, we estimated how the accuracy of reconstructions can be improved by gradually incorporating corrections for all these effects. In our investigations, we didn’t perform corrections for the limited camera spatial resolution assuming that the boundaries of the studied object are not known.

Quantitative analysis of the reconstruction results addresses the following questions:

- What is the level of accuracy of SPECT quantitation (in terms of total activity and its distribution) that can be achieved in current oncology applications (especially, the focus of this investigation is on the performance of the MLEM algorithm itself)?
What are the possible methods to improve this accuracy? They include an incorporation of corrections for physical effects (attenuation, scatter, and resolution loss) and modifying algorithmic parameters (number of projections and iterations).

2. Monte Carlo simulations
The presented study is based on Monte Carlo simulations with six numeric phantoms. Unlike patient scans and phantom experiments, in digital simulations we precisely know the true activity distribution and, therefore, can compare it with the reconstructed one. In our phantoms (Fig.1), different objects of interest (imitating tumours of different shapes) were located inside the cylinder (reproducing human tissue) with 16cm diameter. The sources in phantoms A-C have rectangular boundaries and differ in their size: 4.5cm (10S), 3.5cm (7S), and 2cm (4S), respectively. Here S is the pixel size which equals to 0.47cm. The objects in models D-F are voxelized spheres with diameters 5.5cm (12S), 4.0cm (8S) and 2.5cm (5S). These sources and cylindrical background were filled with $^{99m}$Tc with concentrations of $37.0kBq/cm^3$ and $3.7kBq/cm^3$, respectively. In all cases we used uniform attenuation map with value of $0.15cm^{-1}$.

Based on these voxelized activity and attenuation distributions, we performed Monte Carlo simulations using SimSET [13] code. Parameters of our modelling were selected to be close to conventional SPECT clinical protocol for identifying of sentinel nodes:

- 64 projections (128*128) over 360°;
- Circular orbit with the radius of rotation 29.8 cm;
- Low energy high resolution (LEHR) collimator;
- 20% energy window around 140keV photopeak [126-154keV].

![Figure 1. 3D models (upper) and 2D central transversal slices of six (A-F) numeric phantoms.](image)

3. Reconstruction methods
To solve the system (1): we applied the standard MLEM iterative procedure:

$$X_j^{(n+1)} = \frac{X_j^{(n)} + \sum_i C_{ij} \sum_k C_{kj} \frac{Y_i}{X_k^{(n)}} + S_j}{\sum_i C_{ij}}$$

where $n$ is a counter for iterations, and $S_j$ is an item added to the forward step to correct for scattered photons.
Table 1. Modifications of reconstruction protocol tested in this study

|                | #1                        | #2                        | #3                        | #4                        |
|----------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Number of projections | 64                        | 128                       | 64                        | 64                        |
| Attenuation map          | True map with scaling factor 0.75 | True map with scaling factor 0.75 | True map with scaling factor 0.75 | True map                |
| Resolution recovery     | 2D Gaussian model [14]     | 2D Gaussian model [14]     | 3D Gaussian model [14]     | 3D Gaussian model         |
| Scatter correction      | No                        | No                        | No                        | $S_i$ is analytically calculated and incorporated into the forward step [15] |
| Post-processing         | 3D Gaussian filter        | 3D Gaussian filter        | 3D Gaussian filter        | 3D Gaussian filter        |

We compared the performance of the four versions of the conventional MLEM algorithm (#1-4) as presented in Table 1. All methods used 128x128x128 image matrix, some form of resolution recovery and attenuation correction. Version #1 performs the simplest slice-by-slice reconstruction with 2D resolution recovery and attenuation correction with attenuation coefficients scaled to the broad beam values to partly correct for scatter. In version #2, we increased the number of projections which resulted in the square system matrix. In the method #3, the camera response was modelled by a 3D Gaussian function with depth-dependent resolution [14]. Modification #4 incorporates scatter component into the forward step of MLEM algorithm. The distribution of scattered photons was analytically calculated by APD [16] method based on the true attenuation map and the activity distribution reconstructed by method #3. While algorithms #1-3 take into account the effect of scatter indirectly (by scaling the attenuation map to the broad beam values), the last method utilizes an analytical distribution of scattered photons estimated with a high level of accuracy [15-16]. Thus, method #4 incorporates corrections for both types of interaction of photons with tissues (attenuation, scatter) and for detector related effects (collimator blurring). In our opinion, the last three modifications represent what could be potentially clinically meaningful, yet very practical (i.e. relatively easy implementable in the clinical environment) improvement to the currently used algorithms.

Our experiments included multiple reconstructions. Every version (#1- #4) of the MLEM algorithm was applied to all numerical models. In total, 500 iterations were performed for every case. At each iteration, the reconstructed images were visually and quantitatively examined. We used two figures of merit to assess the accuracy of the reconstructed images: relative total activity ($RTA$) and relative absolute deviation ($RAD$) which had been defined in the following manner:

$$RTA^{(n)} = 100\% \cdot \frac{\sum_{j \in \Omega} X_{j}^{(n)}}{\sum_{j \in \Omega} X_{j}^{T}}$$  \hspace{0.5cm} (3)$$

$$RAD^{(n)} = 100\% \cdot \frac{\sum_{j \in \Omega} |X_{j}^{(n)} - X_{j}^{T}|}{\sum_{j \in \Omega} X_{j}^{T}}$$ \hspace{0.5cm} (4)$$

where $X_{j}^{(n)}$ - solution of the system (1) after $n$ iterations, $X_{j}^{T}$ - truth, $\Omega$ - area of sources (objects of interest, Fig.1). The $RTA$ shows the ratio of the total activity inside the volume of interest (VOI) to
the true total activity. The RAD indicates how close is the distribution $X_j^{(n)}$ within VOI to the truth $X_j^T$.

4. Results

4.1. Convergence behaviour

Figure 2 presents the results of our analysis of the convergence behaviour of functions $RTA^{(n)}$ and $RAD^{(n)}$, for each method (#1-4) and for each phantom A-F (Fig.1) for up to 500 iterations for any single case. The upper row shows the comparison between RTAs pertaining to the simplest algorithm #1 and its most sophisticated modification #4. One can notice that the convergence of $RTA^{(n)}$ for each considered case has asymptotic behaviour. The value that $RTA(500)$ reaches after 500 iterations increases with the size of the objects. Moreover, the same value of $RTA$ is reached faster (after fewer iterations) for sources with smaller size. The 3D resolution recovery and scatter corrections implemented in the procedure #4 improved the reconstructed total activity inside sources $\Omega$: the dashed line (Fig.2) corresponding to this algorithm is higher that the solid one related to method #1 for all examined cases.

The lower row in Figure 2 displays the dependence of the relative deviation $RAD^{(n)}$ on the iterations counter $n$. For each of the curves the number of iterations $N$ corresponding to the point where $RAD^{(n)}$ attained its minimum was identified for each source and each reconstruction method. Comparing solid (or dashed) lines pertaining to models A-F, one can observe better RTA values for larger objects obtained by one and the same algorithm. For any single model, method #4 (dashed line) has lower minimum value $RAD^{(n)}$, but this ratio might change if calculations continue (columns A and E).

In Table 2 and Figure 3 we compared the solutions received after (i) “optimal” number of iterations $N$ and (ii) 500 iterations.

4.2. Influence of different corrections

When comparing the values of $RTA^{(n)}$ and $RAD^{(n)}$ obtained by methods #1 and #2 corresponding to different numbers of projections, only small improvement (less than 1%) for “large” and “medium” objects can be observed. For small sources, this doubling of camera projections led to the variations at levels of 2-3%. Incorporation of the 3D resolution recovery (algorithm #3) improved the quantitative...
accuracy of the reconstruction up to 6%, scatter correction (method #4) improved it additionally up to 3%. These results prove that 3D resolution recovery can be identified as the most important correction to improve accuracy of estimating RTA. Incorporation of scatter correction in the forward step of the MLEM algorithm can potentially allow users to decrease the number of iterations: the optimal number of iterations $N$ for method #4 is less than for method #3 (column 2, Table 2).

### Table 2. Relative total activity (RTA) and relative absolute deviation (RAD) pertaining to sources A-F and reconstruction methods #1-4.

| Model          | “Optimal” number $N$ of iterations with minimal $RAD^{(N)}$ | $RTA$ after $N$ iterations $RTA^{(N)}$, % | $RTA$ after 500 iterations $RTA^{(500)}$, % | $RAD$ after $N$ iterations $RAD^{(N)}$, % | $RAD$ after 500 iterations $RAD^{(500)}$, % |
|----------------|-------------------------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| **Model A (“Large Cube”), 891 voxels** |                                                                 |                                          |                                          |                                          |                                          |
| Method #1      | 70                                                          | 67.6                                     | 70.9                                     | 33.6                                     | 45.3                                     |
| Method #2      | 92                                                          | 68.2                                     | 70.7                                     | 32.9                                     | 38.6                                     |
| Method #3      | 70                                                          | 71.0                                     | 75.4                                     | 31.4                                     | 42.6                                     |
| Method #4      | 62                                                          | 71.7                                     | 77.2                                     | 32.1                                     | 47.6                                     |
| **Model B (“Medium Cube”), 441 voxels** |                                                                 |                                          |                                          |                                          |                                          |
| Method #1      | 146                                                         | 64.7                                     | 67.6                                     | 36.9                                     | 41.8                                     |
| Method #2      | 150                                                         | 64.4                                     | 67.1                                     | 37.1                                     | 41.2                                     |
| Method #3      | 176                                                         | 69.5                                     | 72.5                                     | 35.0                                     | 38.2                                     |
| Method #4      | 164                                                         | 72.2                                     | 75.8                                     | 35.6                                     | 41.7                                     |
| **Model C (“Small Cube”), 45 voxels** |                                                                 |                                          |                                          |                                          |                                          |
| Method #1      | 332                                                         | 49.6                                     | 50.8                                     | 51.9                                     | 52.6                                     |
| Method #2      | 484                                                         | 52.7                                     | 52.7                                     | 48.1                                     | 48.1                                     |
| Method #3      | 264                                                         | 53.1                                     | 55.4                                     | 49.1                                     | 49.6                                     |
| Method #4      | 180                                                         | 55.6                                     | 59.9                                     | 46.7                                     | 48.3                                     |
| **Model D (“Large Sphere”), 949 voxels** |                                                                 |                                          |                                          |                                          |                                          |
| Method #1      | 54                                                          | 69.6                                     | 71.7                                     | 31.5                                     | 42.4                                     |
| Method #2      | 70                                                          | 69.9                                     | 71.3                                     | 31.1                                     | 36.6                                     |
| Method #3      | 60                                                          | 72.6                                     | 75.3                                     | 30.3                                     | 40.7                                     |
| Method #4      | 46                                                          | 72.9                                     | 76.8                                     | 31.1                                     | 46.0                                     |
| **Model E (“Medium Sphere”), 437 voxels** |                                                                 |                                          |                                          |                                          |                                          |
| Method #1      | 94                                                          | 65.8                                     | 68.0                                     | 35.1                                     | 44.0                                     |
| Method #2      | 106                                                         | 65.8                                     | 67.5                                     | 35.4                                     | 40.2                                     |
| Method #3      | 104                                                         | 69.9                                     | 73.1                                     | 33.7                                     | 43.5                                     |
| Method #4      | 98                                                          | 72.7                                     | 76.7                                     | 33.5                                     | 47.8                                     |
| **Model F (“Small Sphere”), 57 voxels** |                                                                 |                                          |                                          |                                          |                                          |
| Method #1      | 118                                                         | 49.2                                     | 50.2                                     | 52.2                                     | 55.8                                     |
| Method #2      | 270                                                         | 51.8                                     | 52.2                                     | 49.5                                     | 50.2                                     |
| Method #3      | 88                                                          | 56.1                                     | 59.5                                     | 47.6                                     | 56.5                                     |
| Method #4      | 68                                                          | 58.6                                     | 65.1                                     | 45.6                                     | 57.0                                     |
4.3. Comparison of different sources
A comparison of central transversal slices of the best (in terms of minimal $RAD$) images reconstructed by methods #1 and #4 with the truth is presented in Figure 3. The algorithm #4 demonstrates a noticeable improvement over simple method #1 for small sources C and F which is also confirmed by the RAD values shown in Table 2. Nevertheless, even the most sophisticated #4 version of the MLEM algorithm cannot accurately reconstruct shapes of these relatively small sources: both images and profiles do not reproduce the difference in shape between sources C and F. All of our medium and large images (phantoms A, B, D, E) have artefacts - non-uniform distributions in the central slices with some “cavity” in the middle of the phantom. These artefacts become more pronounced when the number of iterations increases which is reflected in the increase of relative deviations $RAD$ (Fig. 2).

5. Conclusions
Based on the analysis of images reconstructed from six Monte Carlo simulations by four different methods, the following conclusions can be made:

- Simple reconstruction methods, such as MLEM with attenuation correction and 2D resolution recovery, can achieve the accuracy of total activity ($RTA$) at the level of 70% of the true value for objects with dimensions larger than 7S and at the level of 50% for objects with dimensions 4-5S, where S is the pixel size;
- Practical modification of the current software, which means those that can and are currently being implemented in the clinical environment, such as 3D resolution recovery and
incorporation of scatter correction into forward step of OSEM, can improve the determination of RTA by about 5% for large objects and 15% for small objects;
- The proper 3D resolution recovery constitutes the most important correction to improve quantitative accuracy of estimating RAT;
- The convergence of reconstructed total activity ($RTA^{(n)}$) has an asymptotic behaviour, and by increasing the number of iterations one can only improve the estimation of RTA, especially, for small objects;
- The relative absolute deviation ($RAD^{(n)}$) of reconstructed images from the true distributions reaches minimal values at a particular iteration $N$, after what it starts increasing;
- The optimal (corresponding to minimal $RAD^{(n)}$) number of iteration $N$ increases with (i) the decrease of the size of the object; (ii) increase of the number of projections;
- Incorporation of scatter correction into the forward step of MLEM algorithm allows to lower the number of iterations: the optimal (corresponding to minimal $RAD^{(n)}$) number of iteration $N$ for method #4 is lower than for method #3;
- The exact reconstruction of the activity distribution (not only the total activity value) inside a small object represents an unrealistic task under considered conditions. The achievable values of $RAD$ are 30% for objects with dimensions more than 7S and 50% for objects with dimensions 4-5S;
- For relatively large objects (having size more than 7S in our experiments), the number of iterations which are necessary to achieve optimal values of $RAD^{(n)}$ and $RTA^{(n)}$ might be significantly different (Fig.2). A different behaviour of these curves may require a compromise when assessing quantitative accuracy of relatively large objects: small number of iterations results in underestimation of the total activity, but large number of iterations destroys image quality (especially, artefact in the middle may be created, Fig.3). For relatively small objects (having sizes less than 5S), the shape of the source can not be accurately restored.

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