Monte Carlo simulations for therapy imaging

M Ljungberg
Department of Medical Radiation Physics, Clinical Sciences, Lund, Lund University, Lund, Sweden
E-mail: michael.ljungberg@med.lu.se

Abstract. In therapy imaging there is a need to optimize imaging protocols and different correction methods for e.g. photon attenuation, contribution from scatter and other physics-related effects that limits the possibility to achieve accurate quantitative results. Physical phantom studies are important but lack flexibility and are often difficult to make patient realistic. A complement is to simulate the study using a Monte Carlo-based model of the imaging process including accurate description of the interaction processes and a realistic model of the patient and the imaging device. With the Monte Carlo method it is also possible to simulate and calculate parameters that otherwise would be impossible to measure from a physical experiment. An example of such is the simulation of a scatter and an attenuation-free situation. Results from such simulations can be very important in a validation procedure serving as reference data for which results obtained by different correction methods can be compared to. The Monte Carlo method has also been used to calculate absorbed doses from reference phantom or patient-specific phantom obtained from a CT study. This paper give an overview of the method and show examples of how Monte Carlo simulation can be used to evaluate therapy imaging with different radionuclides but also how simulations can be used for calculation of necessary parameters for correction of scatter, attenuation and collimator response.

1. Introduction
Selection of radionuclides for radionuclide therapy is, of course, optimized for a successful treatment and as a consequence these radionuclides are not always suitable for imaging with scintillation cameras. Limit factors can be multiple high-energy photon emissions or low emission abundances which can leading to noise problems. Nevertheless, imaging of on-going treatment can provide important information about the outcome of the treatment and also provide a verification that the predicted absorbed dose actually is delivered to the target volume and that normal organs/tissues, that are regarded as risk-organs, receive an absorbed dose that is acceptable and below levels for side-effects. In order to develop a proper method for quantification of activity it is important that the underlying problems are fully understood. A very useful tool to gain such knowledge is the Monte Carlo method. From Monte Carlo simulations, important parameters and imaging characteristics can be quantified and visualised and used to both develop and verify compensation methods. In this paper, we will discuss the application of Monte Carlo for the radionuclides $^{177}$Lu, $^{131}$I and $^{90}$Y that are commonly used for different types of radionuclide therapies.
2. The Monte Carlo method
The Monte Carlo method is a statistical method that from random numbers perform simulation of stochastic problems using computers [9]. In medical imaging, the transport of particles (i.e. photon and electrons) can be simulated by a model of the system and the physical processes by sampling of probability density functions (pdf's). When comparing to experimental studies, Monte Carlo simulations have several advantages. Firstly, it is easy to modify the system and thus investigate the corresponding effect on the characteristics of the system. Secondly, it is possible to investigate parameters that are virtually impossible to measure. Examples of such parameters are the contribution to an image from photons scattered in the patient and the fraction of photons penetrating the collimator septa. Hence, a Monte Carlo program can provide information when developing correction methods since the physical processes generally in detail are known and components in, for example, an image can be separated allowing for studies of the relative importance of different effects.

There are several public-domain Monte Carlo programs available that can be used for Monte Carlo simulation of nuclear medicine imaging. The Gate program is a Monte Carlo program based on the Geant4 simulation toolkit and has been developed for tomographic applications [7]. It is based on a script-language and has a powerful geometry package making it very suitable for tomographic camera design for both SPECT and PET. EGS4 [12] and MCNPX [1] are programs mainly developed for high-energy physics but have capabilities of simulating imaging systems. At Lund University, we have developed the SIMIND code which is a Monte Carlo program dedicated for simulation of scintillation detectors, scintillation cameras and SPECT [8]. This program has been used in the following examples.

3. The scintillation camera
A standard scintillation camera consist of a NaI(Tl) crystal, a collimator of lead (mostly a parallel hole design) and a large set of photo-multiplication tubes (PMT) connected to position-recording electronics. When photons interact in the crystal, excitations occur with scintillation light emission. This light is guided to and collected by the PMT’s to form an energy signal. The position of an interaction is determined by the energy signals from the different PMT’s weighted by their spatial position. If the sum of the energy signals passes the energy discriminator the x,y position will be digitized and stored in an image matrix.

3.1. Planar imaging
A scintillation camera is a 2D imaging modality where images are created from photon travelling along rays (projections). This has some serious implications on the image mainly because no depth-information can be resolved. Contribution from overlapping and under-lapping activity can therefore mask small volume-of-interests making detection of small lesions impossible. The spatial resolution get worse at larger distances due to the design of the collimator which leads to loss in image contrast for sources distant to the camera surface. Furthermore, proper attenuation correction can be a problem.

3.2. SPECT
To overcome these problems, tomographic methods have been developed. The principle for SPECT (Single-Photon Emission Computed Tomography) is to measure planar images in different projections and from these projections reconstruct 3D tomographic images. Most methods used today in the clinic are based on the iterative MLEM/OSEM algorithms where projections of an initial guess of the activity distribution are determined iteratively from a relevant model of the imaging process in a forward projector step. Error projections are then obtained from the quota of the measured projections and the calculated projections. These error projections are back-projected to form an error image used to update the initial guess. This procedure continues until convergence has been reached. The differences between the MLEM and the OSEM algorithms are mostly related to when and how many stages, during a particular iteration, the estimate of the image should be updated since the error image in an OSEM method is calculated only from a subset of projection angles.
3.3. Photon attenuation
Measured projections are affected by non-homogeneous photon attenuation in the patient resulting in too low count values in the projections. The photon attenuation is generally a function of photon energy, body composition, density and on the source location. In non-homogeneous regions, such as the thorax, this makes it a complex radiation transport problem to solve. Since an iterative algorithm aims to find an image solution for which related projections converge to the measured projections, it is important that the model of the camera in the projector step also includes modeling of the attenuation.

3.4. Scatter contribution
The underlying reason for an unwanted scatter contribution in the image is that NaI(Tl) scintillation cameras do not measure imparted energy very well. The energy resolution (i.e. the statistical uncertainty in the energy signal) is about 10% (FWHM) at 140 keV. This means that a relative large energy window will be needed to maintain good counting statistics. If compton scattering occurs in the patient with only a slight change in energy and direction, there will be a chance that events from those photons are accepted within the energy window due to the energy resolution. These events are, however, to some degree miss-placed resulting in a decreased images contrast. Quantitative imaging is also difficult to perform since the scatter contribution and its spatial distribution is non-linear.

3.5. Collimator response and septal penetration
The underlying design of a parallel collimator is the main reason for the poor spatial resolution in scintillation camera imaging. Since photons initially are emitted in an isotropic direction, then the principle for geometrical collimation imply that a narrow collimator hole (better spatial resolution) will lead to fewer detected counts (a lower sensitivity) for a given activity and acquisition time. The poor spatial resolution also makes it difficult to quantify activity concentrations in small volumes. This limits the accuracy, for example, regarding tumor dosimetry. Furthermore, collimators are optimized for particular photon energies. This introduces a problem if additional photons with higher energies than the principal energy are emitted during the decay. For these photons, the collimator septa might not be sufficiently thick to guarantee a high fraction of photon absorptions. The results will be septum-penetration with a result in a point-spread function of long wide tails and characteristic streaks that match the flat sides of the hex-holes. The result in the image will be a lower contrast and counts outside the patient.

4. Corrections needed for therapy imaging
Today, most quantitative correction methods are implemented in some kind of iterative reconstruction method since the projector/backprojector is a natural stage in implementing the degrading effects that occur in real measurements. It should be remembered that the reconstruction processes try to find a distribution for which its calculated projections are as close as possible to the real measurements. Implementation of physical effects in the projector/backprojector will, in reality, mean a correction for the effects. Monte Carlo simulations are very important when validating correction methods because it is possible to simulate images of a clinically realistic activity distribution without any photon interactions in the phantom. Thus, those images will represent the case of perfect correction methods and therefore are very useful as reference images. Measurements using physical phantoms are also possible for comparison but the problems with this type of measurements are in the somewhat limited flexibility in making clinical realistic images. Furthermore, realistic physiological movements with a high degree of realism can be hard to implement on a physical phantom.

4.1. Compensation for photon attenuation
Compensation for attenuation is relatively easy to implement in the forward projector. Today, usually such information is obtained from a registered CT study. One problem here is to properly convert the data from the Hounsfield voxel numbers (which is obtained from a spectrum of x-ray photons) to linear attenuation coefficients that reflect discrete photon energies. Another potential problem today,
with modern hybrid SPECT/CT systems is that images obtained from a fast CT acquisition do not always reflect the ‘average’ attenuation caused by the patient’s breathing. It should be remembered that SPECT data is acquired over a long time period in which the patient breathe. Therefore, an attenuation map should reflect the average of the respiratory motion and not a snapshot.

4.2. Compensation for scatter

Scatter correction is somewhat more complicated to compensate for as compared to attenuation. Monte Carlo simulations have been shown to be very useful to understand the scatter characteristics (qualitatively and quantitatively) since it is impossible to properly measure only scatter in the main energy window. Most compensation methods are based on either acquisition of scatter estimates from multiple energy windows or modeling scatter distribution, analytically, directly in the reconstruction algorithm. The most common energy-window method is probably the triple-energy window method where two narrow energy windows are placed on each side of the main energy window and a scatter images is obtained from a weighted average of the two related scatter images. Energy-window based methods are relative easy to implement by do not always reflect the scatter in the main peak properly because events from photon scattered with different number of orders appear in different parts of the measured energy spectrum. Most of the scatter in the main energy window usually comes for single-order scattered photons that have been scattered in very narrow angles and therefore only loose a small fraction of their energy. To reduce noise problems, scatter window data can be implemented in an iterative algorithm as an additive component rather than be subtracted from the SPECT projections prior to reconstruction. The ESSE method [5] is an example of an algorithm where Monte Carlo simulated scatter kernels as function of depth are used to model the overall scatter distribution. It is also possible to implement full Monte Carlo simulations to estimate the scatter. Such work has been published for ⁹⁹mTc and ¹³¹I [2]. These sophisticated approaches are expected to provide the best quantitative accuracy and include Monte Carlo simulation of compton scattering.

4.3. Compensation for collimator-response

The poor spatial resolution caused by the collimator can partly be compensated for by introducing a distance-dependent blurring in the projector step. If no penetration occurs a gaussian-shaped distance-dependent model of the blurring can be used. However, septal penetration introduces non-symmetrical Point-Spread Functions (PSF) with distinct penetration streaks. A way to account for this is to use pre-Monte Carlo calculated PSFs using Monte Carlo simulations and store these kernels as a function of distance [4]. Monte Carlo simulations do allow for calculations of the fraction of events in the image originated from photons penetrating the septa. This information can be very useful, particular in collimator design for radionuclides used for therapy. For ⁹⁹mTc, these procedures with forced-detection of photons for fast collimator simulations has shown to be clinically practical but for more complex decay schemes, such as ¹³¹I, it is also necessary to include scatter in the crystal and in the camera housing, and therefore these forcing methods may be difficult to be used.

5. Monte Carlo simulations of therapy imaging

Below, the examples for ¹¹¹In, ¹⁷⁷Lu, ¹³¹I exemplify the unique possibilities with Monte Carlo simulations. A standard NaI(Tl) scintillation camera with both a MEGP and a HEGP collimator and with an energy resolution set to 10% (FWHM) at 140 keV was simulated. The XCAT anthropomorphic voxel-based computer phantom [13] was used. Figures 1-3 show in column (a) images from geometrically collimated photons that they have not interacted in the phantom or in the camera head (except for the crystal). Column (b) show images from attenuated photons but not scattered in the phantom. No events from septal-penetration or interactions in the camera are included. Column (c) show images from attenuated photons that may have penetrated the collimator septa and scattered in the crystal. Column (d) includes, in addition to the previous case, also photons scattered in the phantom. Finally, column (e) show images with all events including backscatter. Poisson noise has been added to all images in order to reflect a more clinical realistic image.
5.1. $^{177}$Lutethium imaging
This radionuclide, labelled to peptides such as Lu-(DOTA0,Tyr3) octreotate, have demonstrated successful treatment of neuro-endocrinal tumours [6]. The decay includes some photon energies suitable for imaging. The two most important photon energies are 208 keV (11%) and 113 keV (8%). The $^{177}$Lu decay is relatively clean with only one photon emitted with an energy that is higher than the principal energy. The effect of attenuation can clearly be seen in figure 1(b) compared to 1(a), the penetration and scatter do not affect the image quality so much, because the MEGP collimator is optimized for a larger energy than 208 keV. Thus, this radionuclide makes possible to do quantitatively accurate therapy imaging.

![Figure 1](image1.png)

**Figure 1.** The images from $^{177}$Lu photons, which are relatively sharp since few events come from septal-penetration and backscatter in the camera housing.

5.2. $^{131}$Iodine imaging
$^{131}$Iodine has been used for many years in therapy of the thyroid and recently also labeled to antibodies, such as the $^{131}$I-tositumomab for treatment of lymphomas. The $^{131}$I decay includes a photon with the energy of 364 keV (80%) which makes therapy imaging possible. However, there is also emission of additional photons of higher energies which significantly affect the image quality. The two most important energy are 637 keV (7.3%) and 722 keV (1.8%).

![Figure 2](image2.png)

**Figure 2.** Images of $^{131}$I showing some patterns caused by the collimator holes. The events from septal-penetrated (c) scattered photons and (d) backscatter photons (e) appear as a blurred effect on the image quality.

Dewaraja et al. have used the Monte Carlo method to characterize the images obtained from $^{131}$I-labelled monoclonal antibodies [3]. Due to the complexity of the decay and the interaction within the camera, they have also investigated methods for a full Monte Carlo simulation of the scatter contribution implemented in an iterative reconstruction procedure [2]. The program SIMIND was used and the approach was that scatter, estimated in form of simulated images, is calculated at different iterations by exporting the estimate of the tomographic image, together with the patient’s registered CT image to the Monte Carlo program, to perform an extended simulation including penetration in the collimator and backscatter in a compartment behind the crystal.

5.3. $^{90}$Ytrrium imaging
This radionuclide is a candidate for radionuclide treatment due to its large $\beta$-particle energy (and related particle range). One problem is that no $\gamma$-photons are emitted in the decay. However, during the $\beta$-interaction with surrounding tissues, bremsstrahlung photons can sometimes be emitted which can be detected by a scintillation camera. A major problem is, however, that bremsstrahlung photons spans in energy from the maximum $\beta$-particle energy down to very small energies. There is, thus, not a
distinct photo-peak in the energy spectrum. This implies difficulties when defining which events should be regarded as ‘good’ events. Regardless of energy window position, there will always be a mixture of events coming from photon scattered in the patient, camera crystal and housing, collimator, PMTs etc. together with events from photons that have penetrated the collimator septa. Scatter correction using multiple-energy windows are, therefore, not appropriate. The probability for bremsstrahlung generation per decay is also small leading to noisy images. In our application of bremsstrahlung imaging at the Lund University, ‘good’ events are defined as those resulted from a photon that was not scattered anywhere and that passed the collimator hole geometrically. All other events are defined as ‘bad’ and then Monte Carlo calculated scatter- and collimator kernels are used for compensation within an iterative reconstruction procedure. A consequence of this definition was that the sensitivity could only be obtained from Monte Carlo simulations. Comparison with experimental measurements, however, concluded that a good activity recovery could be obtained [11].

Figure 3. Simulated images of $^{90}$Y bremsstrahlung photons. Upper row shows images simulated with the MEGP collimator and lower row shows images with the HEGP collimator. Note the penetration in (c) and the contribution from scatter in (d).

An implementation of bremsstrahlung imaging applied on data from an ongoing high-dose clinical trial with treatment of B-cells Lymphoma using $^{90}$Y-labeled ibritumomab tiuxetan antibodies imaging has been described by Minarik et al. [10]. The administered activity needed to get the predicted absorbed dose to the main organ-at-risk was calculated from a pre-therapy study with $^{111}$In-labeled ibritumomab tiuxetan antibodies. During treatments with $^{90}$Y-labeled ibritumomab tiuxetan antibodies, several multiple SPECT/CT studies were made by bremsstrahlung imaging. The images were then quantified by correcting for non-homogeneous attenuation, scatter and collimator-response including septal penetration.

5.4. Characterization of events in the energy window

Monte Carlo calculations can help in characterizing the relative contribution to the images. The results in table 1 are from an example of such characterisation, taken from the simulations of such images. We can note that for $^{177}$Lu most events comes from geometrically collimated photons and a small fraction from penetrations. This is because the collimator used is a medium-energy collimator with good absorption probability for 208 keV photons. No back-scatter occurs. However, a significant fraction of events comes from photons scattered in the phantom. For $^{90}$Y, a large fraction comes from photons back-scattered behind the crystal especially for the MEGP collimator. This comes mainly from the high-energy bremsstrahlung photons that are highly penetrating through the collimator and crystal having enough energy to contribute to events in the energy window even though they have been backscattered with a large angle.
Table 1. Characterization of events, registered within the energy window, for four radiopharmaceuticals.

| Type of event                  | $^{177}$Y | $^{131}$I | $^{90}$Y(ME) | $^{90}$Y(HE) |
|--------------------------------|-----------|-----------|-------------|-------------|
| Geometrically collimated       | 68%       | 41%       | 13%         | 19%         |
| Septal penetration             | 4%        | 19%       | 19%         | 10%         |
| Scattering in the phantom      | 25%       | 17%       | 40%         | 49%         |
| Backscattering behind the crystal | 0%      | 9%       | 49%         | 32%         |

There is also a large fraction of events that comes from photons scattered in the phantom. However, this fraction is lower for $^{131}$I than for $^{177}$Lu because scatter is more easily discriminated for higher photon energies (increased separation between the full-energy peak and the Compton edge). For $^{131}$I, there is also a fraction of events from photons penetrating the collimator. These events are most likely coming from the 637 keV and 722 keV photons that after penetration are Compton scattered in the crystal before escaping and contributing to the main energy window with their partial energy deposition.

5.5. Characterization of events in the energy spectrum

It is not trivial to decide where energy windows for scatter corrections should be located when imaging a radionuclide with multiple photon emissions. Photons can be properly collimated but scattered with an escape in the crystal, leading to a ‘good’ registered event with lower energy. Since this event is correctly positioned, a subtraction is, therefore, not a good choice. By separating the events in categories, it is possible from a Monte Carlo simulation to calculate the relative contribution of ‘good’ and ‘bad’ events. Figure 4 and 5 show energy spectrums for each of the above discussed radionuclides. For display purposes, the information in figure 4 is limited to show the total spectrum corresponding to real measurements and the events from geometrically collimated photons that have not been scattered anywhere and, hence, represent ‘good’ events. For $^{177}$Lu, it can be seen from figure 4(a) that scatter in the phantom is the major contributor to unwanted events in the main energy window. In the $^{131}$I case, figure 4(b), it is evident that the high-energy photons, although theoretically with a low abundance, cause a lot of scattering and septal-penetration.

![Figure 4](image-url)

Figure 4. Examples of the $^{177}$Lu (MEGP collimator) and the $^{131}$I (HEGP collimator) energy spectrums, where the ‘good’ events are coming from unscattered photons; the geometrically collimated photons are plotted (solid) together with the total spectrum (dashed-dotted) representing a real measurement.
Figure 5(c) and 5(d) shows the $^{90}$Y energy spectrum for the two collimators. There is much more penetration and scatter when using the MEGP than the HEGP collimator, but there is a relatively small increase in the geometrically collimated photons.

Figure 4. Examples of the $^{90}$Y energy spectrums with the MEGP and HEGP collimators, where the ‘good’ events are coming from unscattered photons; the geometrically collimated photons are plotted (solid) together with the total spectrum (dashed-dotted) representing a real measurement.

7. Conclusion
The Monte Carlo method has shown to be very useful when evaluating imaging properties in both diagnostic and therapeutic nuclear medicine applications. In radionuclide therapy, most of the radionuclides used are not optimal for imaging and they may result in a large contamination of unwanted events, limiting the image quality and reducing the accuracy in quantitative measurements. However, by studying these radionuclides in an imaging situation using Monte Carlo methods, a deeper understanding of the degradation can be gained with a good possibility to develop effective correction methods for most of these effects.

References
[1] Briesmeister J F 2000 MCNP - A General Monte Carlo N-Particle Transport Code v. 4C (Los Alamos, NM: Los Alamos National Laboratory)
[2] Dewaraja Y K, Ljungberg M and Fessler J A 2006 IEEE Trans. Nucl. Sci. 53 181-8
[3] Dewaraja Y K, Ljungberg M and Koral K F 2000 J. Nucl. Med. 41 123-30
[4] Du Y et al 2002 IEEE Trans. Nucl. Sci. 49 668-74
[5] Frey E C and Tsui B M W 1996 Conf. Rec. IEEE Med. Imaging Conf. (Anaheim, CA) pp 1082-86
[6] Garkavij M et al 2010 Cancer 116 1084-92
[7] Jan S et al Phys. Med. Biol. 49 4543-61
[8] Ljungberg M and Strand S E 1989 Comp. Meth..Progr. Biomed. 29 257-72
[9] Ljungberg M, Strand S E and King M A 1998 Monte Carlo Calculation in Nuclear Medicine: Applications in Diagnostic Imaging (Bristol and Philadelphia: IOP Publishing)
[10] Minaik D, Sjogreen-Gleisner K, Linden O, Wingardh K, Tennvall J, Strand S E and Ljungberg M 2010 J. Nucl. Med. 51 1974-8
[11] Minaik D, Sjogreen Gleisner K and Ljungberg M 2008 Phys. Med. Biol. 53 5689-703
[12] Nelson R F, Hirayama H and Rogers D W O 1985 The EGS4 Code System (Stanford: SLAC)
[13] Segars W P, Sturgeon G, Mendonca S, Grimes J and Tsui B M 2010 Med. Phys. 37 4902-15