A Simulation Study of the Counting-Rate Performance of Clinical PET Systems Applying a Methodology for Optimizing the Injected Dose

Nicolas A. Karakatsanis[1], *Student Member, IEEE,* Anastasios Parasyris[1], George Loudos[2], *Member, IEEE*, Konstantina S. Nikita[1], *Senior Member, IEEE*

***Abstract*–The amount of radioactivity injected into patients during clinical PET scans can be critical when designing data acquisition protocols. The objective is to generate projection data with high statistical quality, while the acquisition time remains relatively short and the total amount of injected activity does not exceed a certain level, above which the count losses, due to dead-time effects, become significant. For this purpose an optimal range of total injected activity levels can be determined by employing the performance parameter of the Noise Equivalent Count Rate (NECR). NECR is defined as a metric of the rate in which statistically important coincidence events are counted by a PET system. The NECR depends on the total amount of injected activity and demonstrates a peak value for a certain range of activity levels. However this dependence can be affected by certain patient- and scanner-related parameters causing the shift of the range. Therefore the optimal range can be determined by estimating the NECR response as a function of the activity for a particular scanner-patient system. This is not practical for clinical studies, as it would require the repetition of the method for each patient. In this work we propose an alternative method based on a series of simulations of imaging systems and realistic human phantoms. We used Geant4 Application for Tomography Emission to simulate the independent effect of certain parameters to the NECR. We investigated the relationship between the NECR and the patient size, relative axial position of the patient to the field of view (FOV) of the scanner, combined use of reduced dead time electronics and LSO crystals instead of slow-responding electronics and BGO and finally of the energy window. We used two validated scanner models, three NCAT phantoms, two bed positions and three energy windows. The results show an optimal range of 55-65MBq for HR+ and 300-450MBq for Biograph, when the heart is located at the centre of FOV.**

I. Introduction

The statistical quality of the projection data of a positron emission tomography (PET) scan are related with the rate of true coincidence counts detected by the PET imaging system. The emission of positrons is a Poisson distributed random process. Therefore PET is a statistical imaging technique, where the presence of noise is unavoidable. The objective is to limit the negative effect of noise and improve the statistical quality by increasing the number of detected true coincidences relative to scatter and random coincidences. A possible solution would be to increase the acquisition time, however long scanning periods may not only cause discomfort to patients but result in the reduction of the total number of PET scans performed daily by a PET facility. An alternative option would be to increase the total injected activity, resulting in a higher rate of positron annihilations and consequent gamma emissions. However higher activity levels are not necessarily associated with higher statistical quality due to increased random coincidences and counting losses caused by the dead-time and pile-up effects on detectors. On the other hand, lower activity levels might not induce high enough count rates to ensure a statistically important projection data set for the acquisition times required by modern clinical protocols. Thus, if one considers the total amount of injected activity as a variable, a trade-off is observed between the statistical quality of the projection data and the acquisition time. However, this observation also implies the existence of a short optimal range of activity level values, where the counting rate response of a PET system is high enough to ensure the acquisition of projection data of relatively good statistical quality in a relatively short acquisition time and thus satisfying both contradicting requirements of modern clinical nuclear medicine. In order to determine this optimal activity range, we first need to characterize and quantify the counting rate performance of a PET imaging system. Therefore in this study we have introduced the parameter of the Noise Equivalent Count Rate (NECR) which is applied as a metric of the statistical quality of the coincidence counts per unit scan time.

In this study we use the term "injected dose" to refer to the total amount of activity or activity level injected into a patient before the scan. Therefore, the optimal mean dose range for a particular patient-scanner system is defined in this work as the range of the activity levels required to be injected to that patient in order to induce a maximal NECR value.

The optimal dose range may be different for each patient and is depending mainly on the size and the geometry of the attenuating media of the patient volume relative to the scanner. Ideally the curve of the NECR versus the injected dose should be calculated for each patient in order to estimate the optimal dose range prior to injection. However this method

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N. A. Karakatsanis, K. S. Nikita and A. Parasyris are with the Department of Electrical and Computer Engineer, Biomedical Simulations and Imaging Laboratory of the National Technical University of Athens, 9 Iroon Polutechniou St., 15780, Athens, GR

G. Loudos is with the Medical Instruments Technology Department of the Technological Educational Institute of Athens, Ag, Spyridonos Street, Egaleo, 122 10, Athens, GR

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cannot be applied in clinical studies because it would require a very long acquisition time, which can have negative effects on both the patient and the clinical facility as already explained. Moreover, the activity distribution over the patient body is changing significantly over long scanning periods, resulting possibly in significant variations of the activity present in the FOV at each bed position.

Many studies have considered evaluating the performance of a clinical scanner by estimating a NECR response curve [2-5]. A characteristic example is the National Electrical Manufacturers Association (NEMA) NU 2-2001 standard which suggests the use of a simple cylindrical phantom to model the human body when the NECR performance of a system is evaluated [6]. Furthermore, in most of the NECR studies, relatively simple body-like phantoms have been used in simulations and experiments to construct fixed statistical prediction models, whose results were later simply extrapolated to human studies without sufficient validation. In fact the human body consists of many layers of different attenuation index each and simple anthropomorphic phantoms based on basic geometric volumes cannot provide results that can be safely extrapolated to clinical studies.

More recent studies have shown that NECR can be calculated through a series of appropriate phantom measurements or simulations and expressed as a function of the singles rate, which is largely independent of the geometry and size of the scanned object. Thus, such a methodology would potentially generate a unique NECR response curve as a function of the singles rate for a particular system configuration regardless of the patient scanned and therefore eliminate the need to repeat the method for each patient. A region of optimal singles rate values, where the maximum NECR is achieved, can be determined. Since the singles rate is independent of the size of the scanned object, the previously determined optimal range of single rate values is valid for any type of patient scanned at the specific PET system provided the same system settings are selected every time. During any scan, the singles rate can be monitored on-line by the system and the dose injected can be regulated so that the singles rate induced by the administered dose lies within the optimal range [7]. Recent advances in clinical systems reconstruction software currently allow the direct measurement of the scatters fraction and the randoms and, therefore provide a more accurate estimation of the NECR response. Thus the latter methodology enables not only to predict the optimal dose range but also to estimate the independent effect of the patient's size on the NECR of a system [1].

In clinical studies most of the parameters of the digitizer of the PET scanner are set to an optimal value and remain constant. However there exist customized acquisition protocols for specific cases where different parameters, such as energy window settings, are applied. In this case a clinical dose administration protocol designed with the above methodology would fail, as it requires that all the digitizer settings of the scanner are identical with those selected when the NECR curve versus the singles rate was first estimated. A possible solution would be the construction of multiple NECR curves by repeating the previous method for each new configuration. This might not be practical if many different configurations are to be examined. Moreover this method requires that singles rate is measured on-line during the dose administration of every patient which is also impractical since the dose is usually injected at a separate room away from the scanner several time before.

Hence, a promising alternative methodology would be to simulate an appropriate series of scans with state-of-the-art voxelized anthropomorphic phantoms using a validated model of a scanner system where the affect to the NECR of many parameters both of the patient and the system can be investigated independently to each other. This will allow the prediction of the optimal mean dose range for every patient and system configuration prior to the actual scan.

In this paper we will present a simulation study of the effect of specific parameters to the NECR of a clinical PET system. Thus we will examine the parameters of patient size, relative axial position of the patient to the scanner, energy window length and the type of detectors and electronics used by a scanner. Finally we will propose a simulation methodology to estimate the optimal mean injected dose based on the results and conclusions of the study.

II. Materials and Methods

In this work we selected to use Geant4 Application for Tomography Emission (GATE), a well validated Monte Carlo simulation package, to model a series of scans of NCAT phantoms of varied size and activity. GATE can provide the user with the required trues, scattered and randoms rate data in order to directly calculate the NECR each time. Moreover this simulation package offers the ability to control various digitizer, source, timing and geometry parameters of the simulation and determine the independent effect of each one to the modeled NECR.

Furthermore the NCAT phantom was selected among many other voxelized phantoms because of it's capability to change its size in a homogeneous manner so as to sufficiently reflect the differences in size and geometry of the body of patients with different weight. NCAT is characterized by a detailed representation of both the attenuating volume and the activity distribution of the human torso, allowing the accurate modeling of realistic source and material distributions. All 64 slices from 64^{th} to 127^{th} slice of the original NCAT phantom were included in the simulation. Each slice had dimensions of 96x96 voxels. The activity map was generated by initially setting a uniform background activity concentration over all the tissues of the previous phantom and by later adding a 32 times higher signal activity concentration over the regions of the heart, bladder, kidney and spleen.

The 64 slices were selected so as to cover the human body from the neck to the bladder. This area includes the majority of the tissues that demonstrate relatively high activity uptake

and relatively similar attenuation factors. The brain was chosen to be excluded because of his lower overall attenuation factor whereas the bottom part of the body was not modeled in order to reduce the number of voxels employed and speed-up the simulation. Therefore the activity distributions used in this study were smaller in size than in a real whole-body scan and, given a certain activity concentration for each voxel, the total amount of injected activity is lower by a scale factor compared to actual total activity that should have been injected to a whole-body to induce the same NECR response. For this reason the total injected activity used in the simulation was corrected later by that scale factor to reflect the case of a whole-body clinical PET scan. Consequently all the estimated optimal activity ranges were shifted to higher values before presented in this study. The previously described attenuation and activity maps in transaxial, sagittal and coronal view are presented in Fig. 1 and 2 respectively.

Indeed, the combination of GATE and NCAT model tools provided to this study a flexible and stable environment where the user had the power to control any scanner or patient parameter of his choice.

Figure 1. Transaxial (left), sagittal (center) and coronal view of the central slice of a large NCAT phantom (attenuation map)

Figure 2. Transaxial (left), sagittal (center) and coronal view of the central slice of a large NCAT source distribution (activity map)

The NECR value for each of the following acquisitions was calculated by the following equation:

$$NECR = \frac{T^2}{T + S + (k+1)R} \quad (1),$$

where T, S and R are the mean true, scattered and random coincidence event rates respectively. The factor k indicates the method applied to estimate the randoms and can accept values between 0 and 1, where near 0 values imply the estimation of randoms based on the singles rate and near 1 values indicate an estimation method based on an unsmoothed delayed sonogram without interpolation.

In this study the parameter of NECR was estimated by Eq. (1) after setting *k=0* based on the simulated trues, scattered and randoms rate that were modeled with GATE. Thus the following equation was applied:

$$NECR = \frac{T^2}{T + S + R} \quad (2)$$

First of all two commercial clinical PET systems of different generation of electronics and type of detectors have been chosen to be modeled for this study so as to comparatively evaluate their NECR performance as a function of the injected dose. For this reason, we used two already validated GATE models of the Biograph LSO PET/CT and the ECAT EXACT HR+ BGO PET scanners

The Biograph scanner is equipped with LSO detectors and Pico-3D electronics allowing the system to operate with a relative short dead-time detector response. On the other hand the HR+ has BGO detectors and older generation electronics with 5 times longer dead-time response compared to the Biograph. The comparative study of these systems will provide a clear assessment of the significant improvement of new generation electronics in terms of NECR performance and illustrate how this performance enhancement affects the optimized dose. In Fig. 3 the geometry configuration of the model of Biograph and the relative bed position of a large NCAT phantom are illustrated using the GATE visualization tool.

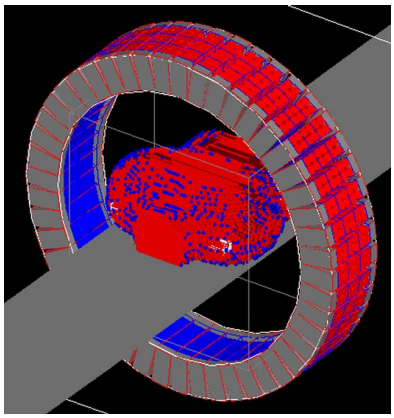

Figure 3. Visualization of the geometric configuration of the GATE model of Biograph 6 and the relative position and size of the NCAT anthropomorphic voxelized phantom

Thus, the size of the patient, the bed position relative to the axial FOV of the scanner, the energy window of the system and the combined effect of electronics dead time and detector type, are the parameters that have been independently examined.

Biograph scanner is characterized by a more efficient dead time response and therefore can image activity distributions of relatively higher total activity compared to HR+. Therefore, a range of 10-800MBq and 10-2800MBq of total activity has been used in order to simulate and design the NECR curve versus the total injected dose for the case of the HR+ and Biograph respectively.

Furthermore three sizes of NCAT phantoms (large, medium and small) were generated and studied in correlation with the rest of the parameters investigated. The relative difference between the two long or short rib axes was approximately selected to 15% and the respective activity and attenuation maps are presented in Figure 4. These three NCAT phantoms have been designed to resemble three characteristic sizes of human body associated with three common human body weights. We considered only three sizes because our aim in this study was to investigate the relationship between the patient weight and the optimized mean dose after carefully selecting three representative human body anatomies.

Figure 4. Transaxial view of the central slice of the large, medium and small NCAT phantoms (attenuation map)

Two bed positions were scanned for both systems. Position 1 represents the case where the heart region is located at the center of the axial FOV of each scanner, whereas position 2 refers to the case where the bladder is axially centered. It has been shown that the NECR curve varies significantly for the same patient-scanner system over different bed positions. This is due to the fact that the intensity of the activity distribution is not spatially uniform over the whole body. Therefore when the NECR of a whole body scan is measured, different values will be obtained over different patient beds. Only the measured NECR values from those bed positions where the imaging targets are located should be taken into account. Fig. 5 visualizes the relevant axial position of the NCAT phantom to the axial FOV of the model scanner.

In many cases the lower energy threshold (LET) of an energy window might change in order to either increase the sensitivity of the system by allowing a wider energy spectrum or reduce the noise caused by low-energy scattered gamma rays by narrowing the window. Consequently the NECR of a system would be affected accordingly. In this work, three energy windows with a constant upper threshold of 650keV and varying lower threshold (375,425,450keV) were used for the LSO scanner and for both bed positions. The LET values were selected to be close to the most common values used in clinic. Our aim is to investigate the effect on NECR and indirectly to the optimal mean injected dose when the LET changes. This will allow us to estimate the optimal dose for every possible energy window applied in clinic.

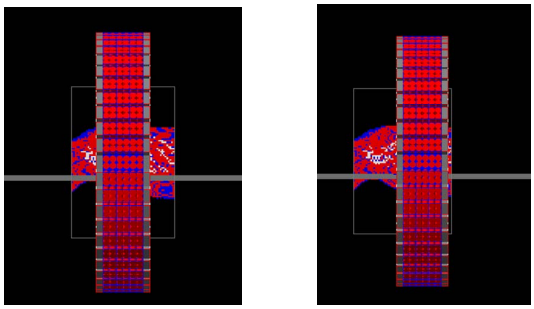

Fig. 5. Sagittal view of the position 1 (left) and position 2 (right), representing the bed position, where the heart or the bladder is located at the center of the axial FOV of the Biograph respectively.

III. RESULTS AND DISCUSSION

First of all the effects of the patient weight on the NECR and the optimal dose range for the Biograph were investigated. As we can see from Fig. 6, the NECR becomes higher, when smaller sizes of NCAT phantom are imaged. This is an expected behavior since the attenuation of the emitted gamma rays is reduced in smaller phantom sizes allowing more trues and reducing at the same time the total number of scattered and randoms.

In the following figures the activity levels ranges are limited to 10-500MBq and 10-1200MBq for the case of HR+ and Biograph respectively in order to illustrate more accurately the behavior of the counting rate response of the systems at these ranges. At Fig. 7 we observe that the dose range, where a NECR value of 90% of its peak value or higher is measured, remains rather constant, despite the changes in patient size. Indeed, the optimal mean dose range for the Biograph is 300-450MBq and has only a weak dependence on the patient body size or weight. Specifically a relatively small decrease of the optimal dose is observed when patient size or weight is increased as it can be seen at Fig. 8. Moreover the relationship between the two parameters can be considered linear. On the other hand a higher degree of linear dependence is observed between the NECR value and the patient size. Simulation results show the relative decrease of the NECR peak value as the patient size increases.

We repeated the same series of simulations for HR+ and observed a weak linear dependence of the same degree between the optimal dose range and the patient size. In figure 9 the NECR curves of a large NCAT phantom for the case of Biograph and HR+ system are plotted together for comparative analysis reasons. The maximal NECR for the Biograph scanner is 8 times higher, while the respective optimal dose is 7 times higher. The use of advanced electronics with 5-times faster dead-time response allows Biograph to achieve higher NECR values for the same amount of dose. Furthermore the maximum NECR corresponds at a significantly higher dose level. The optimal mean dose for the HR+ system lies in the range of 55-65MBq.

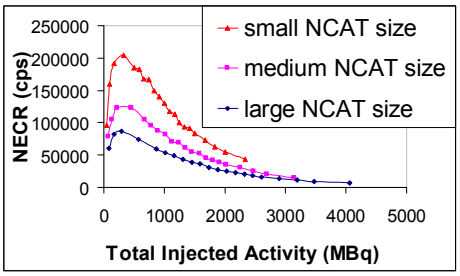

Fig. 6. Biograph NECR vs. total injected dose when three different sizes (small, medium, large) of NCAT phantom sizes have been used, application of the 425-650keV energy window, bed position 1 is selected

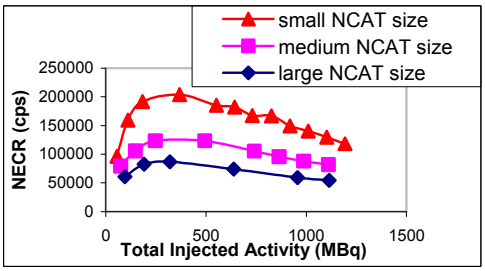

Fig. 7. Biograph NECR vs. total injected dose when three different sizes (small, medium, large) of NCAT phantom sizes have been used (same settings as Fig. 6, except from activity range which has been limited to 10-1200MBq

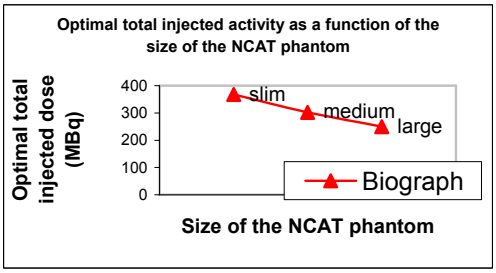

Fig. 8. Estimated optimal injected dose for three different NCAT sizes based on the previous estimation results on Fig. 7

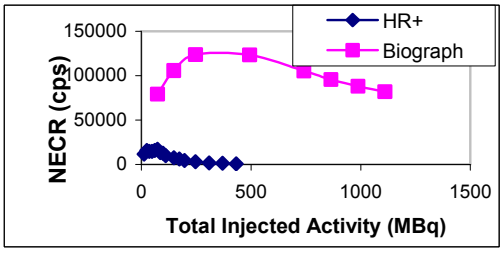

Fig. 9. Comparative diagram of the NECR curve vs. total injected dose for two commercial PET systems: Biograph LSO and HR+ BGO scanner. A large NCAT phantom size has been used with an energy window of 425-650keV, bed position 1 is selected

The energy window of 425-650keV had been selected for all the previous simulation series. In the following section the LET of the window of the Biograph was modified and the respective effects are presented at Fig. 10. When the LET is raised from 425 to 450keV a slightly better NECR value was measured over the entire range of dose levels. On the contrary, when the LET was dropped down to 375keV, resulting in a wider energy window, a fall of the NECR performance was observed because then the system allowed more scattered and random events to be detected compared to trues. On the other hand the optimal dose range does not appear to be affected in any case.

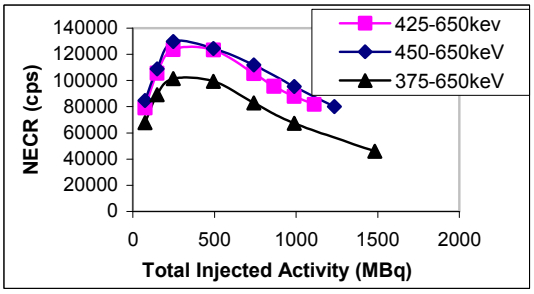

Fig. 10. Biograph NECR vs. injected dose for various energy windows, the medium size NCAT and position 1 have been selected

The axial bed position used in the previous acquisitions corresponded to position 1, where the heart of the NCAT phantom is located at the center of the axial FOV. However, when position 2 is selected and the bladder is shifted to the center of the FOV of the Biograph scanner, the peak NECR of becomes 8 times higher and the optimal mean dose rises to 580MBq according to Fig. 11. On the other hand, the HR+ NECR value becomes 3 times higher and the optimal dose remains insensitive as observed in Fig. 12. The relative lower sensitivity of the HR+ scanner causes the system parameters not to easily get affected by axial shifts.

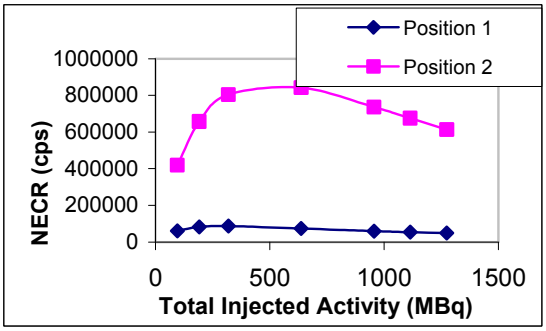

Fig. 11. Biograph NECR vs. injected dose when the heart (position 1) or the bladder (position 2) are located at the center of the FOV, the medium size NCAT and the energy window of 425-650keV has been used

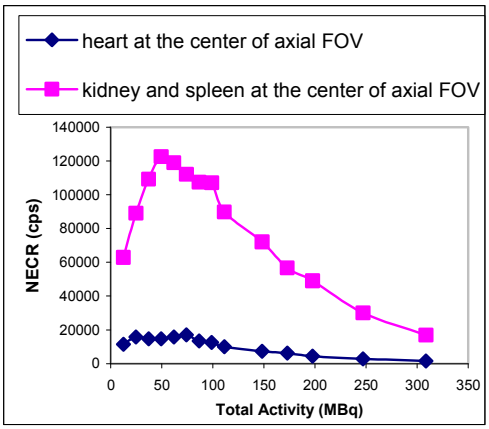

Fig. 12. HR+ NECR vs. injected dose when the heart (position 1) or the bladder (position 2) are located at the center of the FOV, the medium size NCAT and the energy window of 350-650keV has been used.

IV. CONCLUSIONS

In this study we investigated the independent effect of specific patient and scanners parameters on the NECR performance of a clinical PET system. The combined use of GATE simulation software and the NCAT phantom provided us with an ideal powerful environment where certain parameters could be examined thoroughly and their inter-relations could be determined in a straightforward manner.

The design of the NECR curves vs. the injected dose allowed us to determine the mean optimal dose range when phantoms of different size are imaged, when energy windows of different LET are applied, when different bed positions are used and finally when Pico-3D electronics with short dead-times replace older generation of digitizing systems.

We have concluded that the optimal dose is linearly dependent on patient weight but only to a small degree, but it is largely independent of small variations of the energy window length around the standard windows normally used at clinical studies.

Furthermore the bed position can significantly affect the NECR during a whole-body scan, without however affecting the mean optimal dose range that should be administered before the scan.

Moreover the use of LSO detectors together with short dead-time electronics demonstrated a dramatic improvement of the NECR performance. As a result the optimal dose increased by 7 times. However, even with lower dose levels, the NECR performance of modern PET systems is far better than before. Therefore the current generation of electronics allows us to reduce the injected dose and still acquire data with higher NECR and statistical quality.

Finally the above conclusions and the NECR curves vs. injected dose can be further analyzed in order to construct a statistical model that would be capable to estimate in good approximation the optimized dose for every patient based on its size, weight as well as the scanner characteristics and its digitizer settings. We are planning to expand this study in order to investigate more bed positions, energy thresholds and other complex activity distributions. Our aim is to build a reliable statistical model that would be able to predict, in a clinically efficient way and with a certain degree of uncertainty, the optimal dose range for every patient.

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