

A Simulation Study for Optimizing the Injected Dose of Clinical PET systems

Nicolas A. Karakatsanis, Anastasios Parasyris,
Konstantina S. Nikita

Department of Electrical Engineer and Computer Science
National Technical University of Athens
Athens, Greece
knicolas@mail.ntua.gr

George Loudos

Department of Medical Instruments Technology
Technological Educational Institute of Athens
Athens, Greece

Abstract—The optimization of the injected dose in PET imaging systems is important for the design of clinical data acquisition protocols. Methods to reduce the total amount of radioactive dose injected into a patient are investigated. On the other hand, a lower dose may require a longer data acquisition time to obtain images of high statistical quality, thus limiting the total number of PET scans performed by a PET facility per day. Through dose optimization, a compromise between the total dose injected into a patient and the required scan time can be achieved, by ensuring maximum count rate performance for the scanner. In this study, we use the Noise Equivalent Count Rate (NECR) as a metric of the rate in which statistically important coincidence events are counted by a PET imaging system. The optimal dose is defined as the total amount of dose required to be injected into a patient so as to induce a maximum NECR for the particular scanner and patient. Ideally, it can be estimated by determining a curve of NECR versus the injected dose for each scanner-patient system. Recent studies estimate optimal dose for a particular system by expressing the NECR as a function of the singles rate instead. In this work we propose an alternative method based on a series of simulations of imaging systems and realistic anthropomorphic phantoms. We used Geant4 Application for Tomography Emission (GATE) to simulate a series of scans and study the independent effect of various parameters to the NECR of a clinical PET system. We investigated the relationship between the NECR and the parameters of 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 of a system. We used two validated scanner models (ECAT HR+ and Biograph), three NCAT phantoms of different size, two bed positions corresponding to the axial shift of either the heart or the bladder region to the centre of FOV respectively and three energy windows with different low energy thresholds. The results show an optimal mean dose range of 55–65MBq for HR+ and 300–450MBq for Biograph, depending on the patient size, when the heart is located at the centre of axial FOV

Keywords—dose; optimization; Monte Carlo; NECR; PET; Biograph; HR+; NCAT; GATE; weight; clinical

I. INTRODUCTION

The counting-rate response function of a PET system is considered an important performance parameter in clinical scans because it can seriously affect the acquisition time of a scan or the sensitivity and the signal-to-noise ratio (SNR) of

the derived images. The emission of positrons is a Poisson distributed random process. Therefore PET is a statistical imaging technique, where the presence of noise is unavoidable. A possible solution to limit the negative effect of noise and improve the statistical quality of the projection data 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 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 effect on detectors. Thus one can consider a trade-off between the statistical quality of the projection data and the injected dose, implying a short range of dose values where optimal performance can be achieved. In order to determine this optimal dose 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 defined as a metric of the statistical quality of the coincidence counts per unit scan time. It will be 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 calculation of randoms based on the singles rate.

The total dose injected into a patient is proportional to the total activity present in the field of view (FOV) of the scanner. Therefore, the optimal mean dose for a particular patient-scanner system is defined in this work as the amount of activity required to be injected to that patient in order to induce a maximal NECR value for that imaging system.

The optimal dose 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 prior to injection. However this method cannot be applied for every patient because it requires 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. 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 permit now the direct measurement of the scatters fraction and the randoms and, therefore providing a more accurate estimation of the NECR. Thus the latter methodology allows not only to predict the optimal dose range but 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 for every patient and system configuration prior to the actual scan.

In this paper we will present a simulation study of the effect of various parameters to the NECR of a clinical PET system. More specifically 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.

Moreover the NCAT phantom was selected among many other voxelized phantoms because of it's capability to change it's size in a homogeneous manner so as to sufficiently reflect the differences in size and geometry of the body of patients with different weight. Furthermore 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 64th to 127th 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 previously described attenuation and activity maps in transaxial, sagittal and coronal view are presented in Fig. 1 and 2 respectively.



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 (1) based on the simulated trues, scattered and randoms rate.

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

We set $k=0$ because we used the randoms rate result of the simulation instead of estimating it experimentally from an unsmoothed delayed sonogram without interpolation.

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 advancement 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.

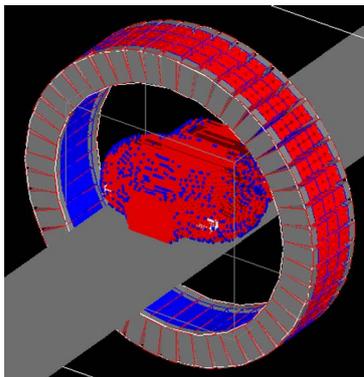


Figure 3. Visualization of the geometric configuration of the GATE model of Biograph 6 and the relative position and size of the NCAT anthropomorphic voxelized phantom

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 much shorter 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.

In addition three sizes of NCAT phantoms (large, medium and small) were generated and combined 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 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.

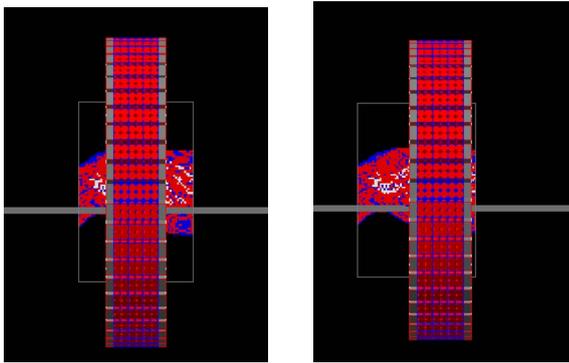


Figure 5. Sagittal view of the position 1 (left) and position 2 (right), representing the bed position, where the heart or the bladder is located at the center of the axial FOV of the Biograph respectively.

III. RESULTS AND DISCUSSION

First of all the effects of the patient weight on the NECR and the optimized dose 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. We also 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 slight increase of the optimal dose is observed when patient weight is decreased. Moreover the relationship between the two parameters can be considered linear.

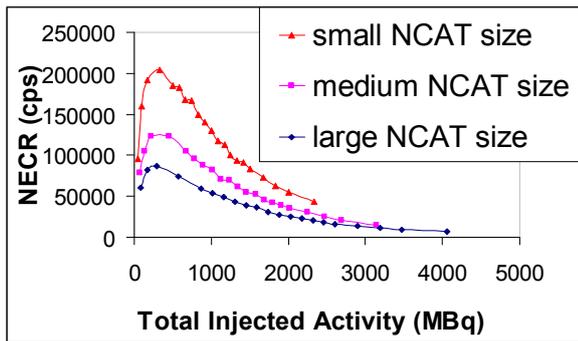


Figure 6. Biograph NECR vs total injected dose when three different sizes (small, medium, large) of NCAT phantom sizes have been used, application of the 425-650keV energy window, bed position 1 is selected

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 7 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.

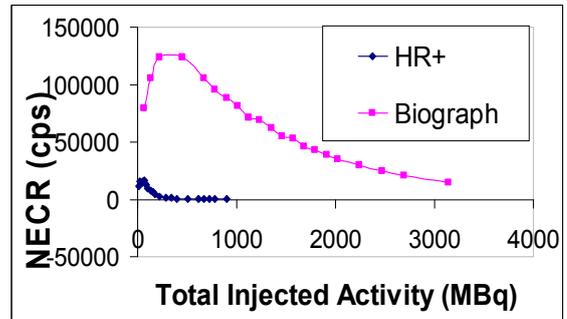


Figure 7. Comparative diagram of the NECR curve vs total injected dose for two commercial PET systems: Biograph LSO and HR+ BGO scanner. A large NCAT phantom size has been used with an energy window of 425-650keV, bed position 1 is selected

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. 8.

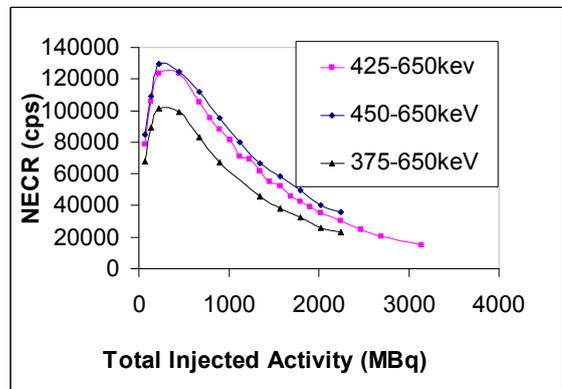


Figure 8. Biograph NECR vs injected dose for various energy windows, the medium size NCAT and position 1 have been selected

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.

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. 9. On the other hand, the HR+ NECR value becomes 3 times higher and the optimal dose remains insensitive as observed in Fig. 10. The relative lower sensitivity of the HR+ scanner causes the system parameters not to easily get affected by axial shifts.

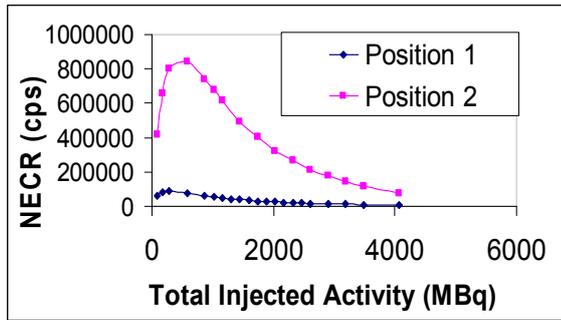


Figure 9. Biograph NECR vs injected dose when the heart (position 1) or the bladder (position 2) are located at the center of the FOV, the medium size NCAT and the energy window of 425-650keV has been used

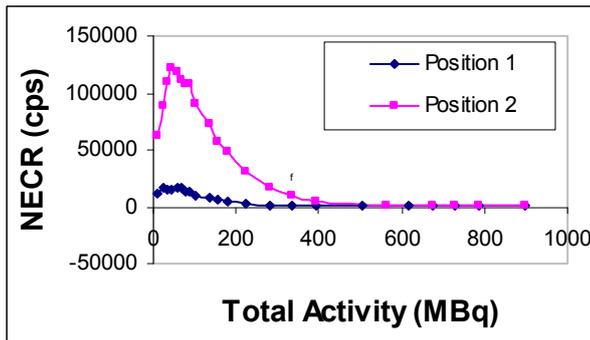


Figure 10. HR+ NECR vs injected dose when the heart (position 1) or the bladder (position 2) are located at the center of the FOV, the medium size NCAT and the energy window of 350-650keV has been used.

Finally at Fig. 10 is presented the plot of the Biograph NECR versus singles rate for the three different phantoms of varying size. This diagram shows the dependence of the NECR by the singles rate which is independent of the characteristics of the object imaged. We observe many similarities between this diagram and the respective NECR curve vs. injected dose presented before. Both diagrams can be used for the estimation of the optimal dose but the methodology which uses the NECR curve vs. injected dose provides direct results without the need for intermediate calculations and scaling of data.

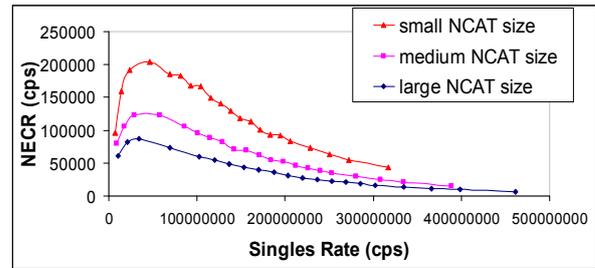


Figure 11. Biograph NECR curve vs singles rate for small, medium and large NCAT phantom volume size, the energy window of 425-650keV has been used, bed position 1 was selected

IV. CONCLUSIONS

In this study we investigated the independent effect of many critical 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 various 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.

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, age 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.

ACKNOWLEDGMENT

The authors would like to thank the OpenGATE collaboration for allowing us to use the GATE simulation software for the purposes of this study. We would also like to thank Arion F. Chatziioannou from the Crump Institute of Molecular Imaging, UCLA for all the valuable insight he has provided us throughout this study.

REFERENCES

- [1] Watson CC, Casey M, Bendriem B, Carney J, Townsend D, Eberl L., Meikle S., DiFilippo F. "Optimizing injected dose in clinical PET by accurately modelling the Counting-Rate response functions specific to individual patient scans", *The journal of nuclear medicine*, vol 46, no 11, Nov 2005
- [2] Bailey DL, Jones T., Spinks TJ, et al, "Noise equivalent count measurements in a neuro-PET scanner with retractable septa", *IEEE Trans Med Imaging*, 1991;10:p256-260
- [3] Stearns CW, Cherry SR, Thompson CJ, "NECR analysis of 3D brain PET scanner designs", *IEEE Trans Nuclear Science*, 1995;42: p1075-1079
- [4] Badawi RD, Marsden PK, Cronin BF, et al, "Optimization of noise-equivalent count rates in 3D PET", *Phys Med Biol*. 1996;41:p1755-1776
- [5] Lartzien C, Comtat C., Kinahan PE, et al, "Optimization of injected dose based on noise equivalent count rates for 2- and 3-dimensional whole-body PET", *Journal of Nuclear Medicine* 2002;43:p1268-1278
- [6] Daube-Witherspoon ME, Karp JS, Casey ME, et al. "PET performance measurements using the NEMA NU-2 70-cm long test phantom for PET", *IEEE Nuclear Science Symposium Proceedings 2001*, M6-6,
- [7] Watson CC, Casey ME, Beyer T, et al, "Evaluation of clinical PET count rate performance", *IEEE Trans Nuclear Science* 2003;50:p1379-1385
- [8] N. Karakatsanis, N. Sakellios, N.X. Tsantillas, N. Dikaios, C. Tsoumpas, D. Lazaro, G. Loudos, C.R. Schmidlein, K. Louizi, J. Valais, D. Nikolopoulos, J. Malamitsi, J. Kandarakis and K. Nikita, "Comparative evaluation of two commercial PET scanners, ECAT EXACT HR+ and Biograph 2, using GATE", *Nuclear Instruments and Methods in Physics Research, Section A*, Vol. 569, Issue 2, pp 368-372, 2006
- [9] P. Gonas, N. Bertsekas, N. Karakatsanis, G. Saatsakis, A. Gaitanis, D. Nikolopoulos, G. Loudos, L. Papaspyrou, N. Sakellios, X. Tsantillas, A. Daskalakis, P. Liaparinis, K. Nikita, A. Louizi, D. Cavouras, I. Kandarakis and G.S. Panayiotakis, "Validation of a GATE model for the simulation of the Siemens biograph 6 PET scanner", *Nuclear Instruments and Methods in Physics Research Section A*, Vol. 571, Issues 1-2, pp 263-266, 2007.