Research Statement

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DESCRIPTION OF PAST RESEARCH STUDIES

Emission tomography imaging has gained considerable attention during the past two decades as a promising technology to obtain three-dimensional (3D) images of the spatial distribution of several important functional characteristics of living organisms. The benefits of this technology were expanded when it became clear that the imaging of life processes could potentially be enhanced by the recording of the spatial distribution over the time domain. Thus, nowadays, specific nuclear imaging techniques employing the principles of emission tomography, such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT), are applied extensively in many highly referenced contemporary medical imaging studies. The scope of their application is ranged from imaging complex molecular processes to performing pre-clinical small animal experimental studies and designing clinical patient scanning protocols.

Parallel to the development of emission tomography imaging systems, techniques are studied, designed, validated and applied for the enhancement of the final reconstructed image quality. The trade-off between multiple competing system performance parameters, such as spatial and time resolution, detection sensitivity, scatter fraction and noise-equivalent count rate is systematically examined in relation to the scanning time and the imaging target geometric and attenuation properties, so as to extract a balanced set of system settings which will allow for the maximal quality in the measured output image signal. The design of the system can be approached as an optimization problem, where several performance parameters should be set such that the statistical quality and, subsequently, the diagnostic information value of the medical image become maximal while certain inherent conditions are satisfied. However, the actual variables of the model we can directly optimize are the geometrical and scintillation properties of the detectors and their relevant position, the type of photomultipliers used, the response of the system's electronics and, to a large extent, the type of algorithms used for acquiring, correcting and reconstructing the raw data.

Numerous experimental studies on a pre-clinical as well as clinical research level have been performed to contribute to the optimal system design that meets specific requirements imposed by each imaging application. Moreover, work is in progress to maximize the efficiency of the algorithms employed for a specific system already developed for pre-clinical or clinical studies. The large set of correlated system parameters and the relatively limited availability of these systems for experimental studies impose certain constraints as to the type, number and duration of experimental studies that can be performed. Therefore, Monte-Carlo simulations can be employed for the realistic modeling of the scanner system response as well as the interaction of emitted particles with matter. The combined use of well validated simulation algorithms with highly detailed 3D voxelized phantoms of small animal or human body can provide a powerful and flexible research tool for the class of imaging studies described previously. On the other hand, due to the inherent complexity of the underlying physical processes undergoing during a PET or SPECT scan and the highly detailed voxelized spatial

distribution of attenuating materials involved, a realistic Monte Carlo simulation algorithm can become very demanding in terms of running time.

During my first year as a PhD candidate at the School of Electrical and Computer Engineering of the National Technical University of Athens, I worked in the development of simulations of clinical PET scanners using a Monte-Carlo simulation software, named Geant4 Application for Tomography Emission (GATE). GATE is based on the well validated Geant4 physics simulation package, which is developed and supported systematically by a large community of scientists in many academic and research institutions across the world. I constructed the models of ECAT EXACT HR+ and Siemens Biograph clinical PET scanners, after successfully validating the simulated performance parameters against those measured in experiments on the actual scanners. For the purposes of validation we estimated the parameters of spatial resolution, scatter fraction, sensitivity and count rate both in simulations and in real measurements using carefully designed experimental set-ups defined in the NEMA NU-2001 standard. Additionally, within the first two years of my PhD program at the same institution, I and my colleagues comparatively evaluated the performance of the two resulting GATE models and determined how the geometry and detector properties of each system affects each performance parameter of the scanners. [1] [2]

The next step in my research plan involved the complete simulation of an imaging study, where I used the already validated scanner models together with a realistic MOBY mouse or NCAT human torso voxelized phantom within a series of carefully designed experiments. Therefore, we constructed one gamma camera with a position sensitive photo-multiplier as well as a four-head small animal PET scanner and then simulated specific scans of a MOBY mouse phantom at both systems. I also developed an algorithm, customized for each scanner, to process the raw simulation data and build a 3D sinogram, which I later processed with STIR software to reconstruct the images using either analytic or iterative algorithms. [3]. Moreover, I further developed the abovementioned algorithm, by adding the capability of processing the raw projection data for the purpose of 3D normalization and attenuation correction techniques prior to reconstruction.

The first research project during my PhD program aimed at the implementation of software programming and Monte Carlo optimization techniques, so as to accelerate the execution of simulation algorithms, especially when voxelized phantoms or detailed physics process models are used. As a principal researcher of the project I worked for 12 months as a visiting researcher at the Imaging Sciences Lab of Crump Institute for Molecular Imaging, UCLA under the supervision of Dr. Arion F. Chatziioannou. I was initially trained in a distributed computing platform at UCLA and then transferred the knowledge I obtained back to my lab, where I built a similar PC cluster for the dedicated parallel execution of simulation and other scientific computational tasks. Monte-Carlo simulations were divided in as many parallel jobs as the available nodes of the cluster, resulting in a maximal speed-up factor of 17. Furthermore, I performed several profiling studies in the simulation code and identified those C++ classes most responsible for the observed execution delay. By applying certain efficiency optimization techniques, I accelerated the execution on a single CPU by 40% approximately both for Geant4 and GATE. The results of this work contributed to the design and completion of more time-demanding simulation studies which would otherwise be impractical, due to the months- or year-long running time required.

Moreover, I was involved in a molecular imaging study, in which we determined the minimum detectable activity (MDA) level of a preclinical LSO PET scanner with intrinsic radioactivity. [4] [5]. Later, I expanded this work for clinical scanners as well [6]. The comparison between the Currie threshold and the estimated detected signal was used as the criteria to determine the MDA performance of the microPET Focus 220 small animal scanner. Furthermore, I have used GATE to model the dose kernels of certain radio-isotopes employed in nuclear medicine for the purpose of a dosimetry study. [7]

During the fourth year of my PhD program I initiated a study, in which I examined the system- and patient-specific parameters affecting the noise-equivalent count rate (NECR) performance of a clinical PET scanner. The NECR is a metric of the statistically significant counts that an imaging system can detect in a unit of time. Therefore high NECR values are highly desirable as they can ensure higher number of detected useful counts in a given scan duration. More specifically I designed a series of simulations, where the simulated NECR of the scanner for various total activity levels was estimated, after changing each time one of the following parameters: the size of the NCAT phantom, the energy window, the bed position and the dead-time response of the electronic acquisition system. The aim of this work is to make generalized conclusions of the effect of each parameter to the NECR performance and to ultimately predict, before the examination, the amount of optimal dose should be injected to patients to achieve the maximal NECR during the scan, based on the current set of parameter values. [8] [9].

Predicting the optimal dose for a specific patient-scanner system, before the radioactive tracer is actually injected into the patient, requires the acquisition of a vast amount of simulated data to achieve a satisfying sampling of the investigated parameters space. Moreover, detailed voxelized attenuation and source distributions as well as low-energy electromagnetic process Geant4 models were employed in order to obtain as realistic NECR diagrams as possible. These two factors increased significantly the total execution time up to one year. However, the parallel execution of jobs at the PC cluster, as well as the optimization techniques applied, helped reducing the required execution time down to approximately one month.

Therefore, the computational speed-up of the simulations allowed this study to expand to a larger set of parameters, while the initially examined space was sampled with a better rate [10]. Moreover, an alternative study was conducted, at which the scan duration was considered a constant, as opposed to the injected dose, which in turn took over the role of the independent variable. Recently, this study was repeated by assigning different scan periods and keeping the dose parameter constant, so as to determine the minimum scan time required per bed position, to achieve a number of noise-equivalent counts higher than a defined threshold value, which ensures an acceptable statistical quality of the projection data [11].

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