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Monte Carlo simulations in SPET and PET

I. BUVAT, I. CASTIGLIONI*

From the Unité 494 INSERM, Paris, France
**INB, University of Milan-Bicocca*
S. Raffaele Hospital, Milan, Italy

Monte Carlo methods are extensively used in Nuclear Medicine to tackle a variety of problems that are difficult to study by an experimental or analytical approach. A review of the most recent tools allowing application of Monte Carlo methods in single photon emission tomography (SPET) and positron emission tomography (PET) is presented. To help potential Monte Carlo users choose a code, we present advantages and disadvantages of the different types of Monte Carlo codes currently available for SPET and PET, discuss common and specific features of the codes, classify the codes with respect to these features, comment key properties for a code to be appropriate for a given purpose and, at last, we consider the possibility of going towards a standardisation of the description of the codes which could facilitate their comparison.

KEY WORDS: Tomography, emission computed - Tomography, emission computed, single photon - Monte Carlo method.

The use of Monte Carlo simulations in SPET and PET imaging

Monte Carlo methods are numerical calculation methods based on random variable sampling. The technique of random sampling to solve mathematical problems has been known since 1770. Only with the advent of quantum mechanics in which matter-radiation interactions were interpreted using cross sections as probabilities, the random sampling technique (named "Monte Carlo method" because the Monte Carlo casino was the most famous centre for playing games involving random drawing) was applied to nuclear physics. In the early 1960s, the Monte Carlo method was used by H. O. Anger to simulate the physical response of his new scintillation camera. Since then, thanks to the possibility of modelling different physical processes independently, the method has been applied in medical radiation physics to a wide range of problems that could not be easily addressed using experimental or analytical approaches. As proofs, an increasing number of scientific papers concerning Monte Carlo studies in nuclear medicine, radiation therapy, diagnostic X-rays as well as radiation protection have come in the scientific literature (Fig. 1).

In Nuclear Medicine, and particularly in SPET and in PET, the use of Monte Carlo methods was advantaged by the possibility of using general purpose codes developed for high energy physics or dosimetry. High-energy (>1 MeV) processes, secondary and low-energy radiations could be neglected as they were not involved in SPET and PET. On the other hand, the similarity of physical and geometrical characteristics of most emission tomographs suggested specific models to be developed thus favouring the creation of codes dedicated to simulations of emission tomography configurations.

Several SPET/PET dedicated Monte Carlo software packages were developed for simulating a variety of

Address reprint requests to: I. Buvat, U494 INSERM, CHU Pitié-Salpêtrière, 91 Boulevard de l'Hôpital, 75634 Paris Cedex 13, France.
E-mail: buvat@imed.jussieu.fr

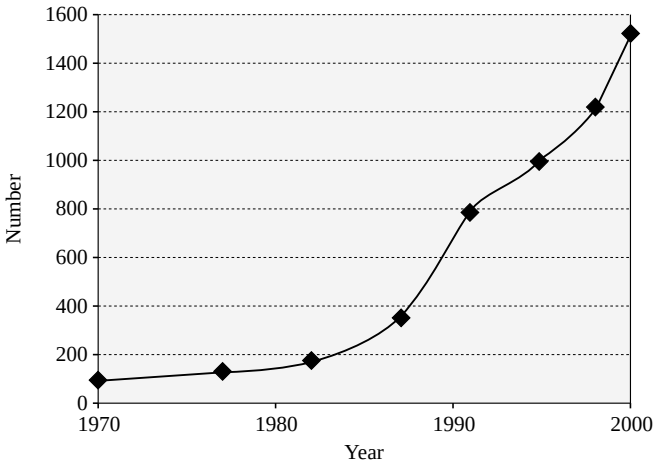

Fig. 1.—Number of published papers on Monte Carlo applications in medical radiation physics from 1970 to 2000.

emission tomography studies. Among them, public-domain codes have been made available in recent years by the newborn Internet web communication, allowing the use of the Monte Carlo method by the whole scientific community and even in the clinical environment.

Several topics were addressed by Monte Carlo simulations in both SPET and PET, among which optimisation of imaging system design (including detector, collimator, and shield design), development of correction methods for improved image quantitation, evaluation of correction techniques (scatter/randoms/attenuation correction, partial volume effect), assessment of image reconstruction algorithms, ROC studies, pharmaco-kinetic modelling.

In this review, we do not present in detail the theoretical aspects of Monte Carlo methods and the results that have been obtained using Monte Carlo simulations in SPET and PET, as these topics have been widely covered in recent reviews and books.[1-5] Our goal is rather to address the practical issues a potential user of Monte Carlo simulations for SPET and PET can encounter. Basically, a new Monte Carlo user or developer has currently free access to a number of Monte Carlo codes. In order to help him to choose which code he should use, we tried to classify the main public-domain Monte Carlo codes by underlying their common and specific features. We also discuss the need to standardise the description of Monte Carlo codes, to help compare the features and performance of current and future codes.

Monte Carlo simulation codes in SPET and PET

Two types of Monte Carlo codes can be used for simulating SPET and PET: 1) general purpose codes, which simulate particle transportation and were developed for high energy physics or for dosimetry, and 2) dedicated codes, designed specifically for SPET or PET simulations.

Modelling SPET and PET configurations using general purpose Monte Carlo codes initially developed to simulate particle transportation in a broad context (like EGS,[6] GEANT [7]) has proven feasible [8-10] and presents several advantages. As they have been designed for a large community of researchers, these codes are well documented and in the public domain. The fact that they are actually widely used (*e.g.*, EGS, developed for radiation dosimetry, is used by more than 5000 persons) results in several valuable characteristics: support regarding the codes can be easily found through user groups, mailing lists, continuing education and Web sites; many of the code components have been extensively tested, hence can be considered as bug-free; although not guaranteed, regular releases, long-term existence and maintenance of the codes can be expected. As computer scientists are sometimes involved in the development of these codes (*e.g.*, GEANT 4), the successive releases can also be expected to make the most of the current programming tools and hardware facilities. However, using general purpose codes for SPET and PET simulations also raise some issues. Indeed, these codes actually include many features irrelevant to SPET and PET (like electron transportation), which inflate the code sizes and complicate their use for specific applications. Learning the code is therefore often tedious, as one has to sort out useful from unnecessary options. In addition, intensive programming is usually required to model SPET and PET, hence validation remains to be extensively performed. As it may not be easy to know *a priori* if the code is well suited to the application of interest, the code features must be carefully examined to make sure that the code is appropriate for simulating the considered configurations.

Dedicated codes, designed especially for SPET and/or PET, could *a priori* be thought more suitable since they are directly concerned with SPET and PET configurations. Indeed, they are usually relatively convenient to implement and learning the use of the code is fast. On the other hand, because the SPET and PET

TABLE I—*Main Monte Carlo codes currently available for SPET and PET simulations.*

Generic codes
EGS4 (radiation dosimetry) [6]
MCNP (radiation dosimetry) [11]
ITS (high energy physics) [12]
GEANT (high energy physics) [7]
Dedicated codes
SPET only:
— SIMIND [13]
— SimSPECT (derived from MCNP) [14, 15]
— MCMATV [16, 17]
PET only:
— PETSIM [18, 19]
— EIDOLON [20]
— Reilhac [21]
— PET-EGS [22]
SPECT and PET:
— SIMSET [23, 24]

community is not as large as communities involved in high particle physics or dosimetry, these dedicated codes are often developed by small research groups, hence maintenance and long-term existence are uncertain. Because the task force involved in the development of these codes is usually rather limited, the codes are also more prone to incomplete documentation, bugs and slower evolution than general purpose codes. As the dedicated codes are often designed with some specific applications in mind, they do not always offer the flexibility that would be necessary to adapt them to the evolution occurring in SPET and PET (modelling transmission acquisition in SPET for instance).

Whether general purpose or dedicated codes should be preferred for SPET and PET simulations obviously strongly depends on the user's needs. Scientists who are not willing to program should favour the dedicated code that best fulfils their requirements. On the other hand, scientists willing to use Monte Carlo simulations for studying original configurations (for instance new detector designs) will find more flexibility and potentialities by considering general purpose codes. Table I summarises the main codes currently available (by internet download or from authors) in each category together with their associated references and Web URL when available.

To determine which code is the most appropriate for a given application, it is important to understand how the codes differ one from another.

What makes Monte Carlo codes different one from another?

All Monte Carlo codes share some common components, such as a random number generator, rules to sample probability distributions, and sets of probability density functions.[4] Here, we rather focus on the features that make the codes different, since knowing these features can help determine which code is best suited to a specific application. These features mostly relate to the accuracy, flexibility, efficiency and ease of use of the codes.

The accuracy of the code mostly depends on: 1) the particle interactions which are simulated and how they are simulated; 2) the components of the detector that are simulated and how interactions in these components are modelled; 3) whether the code has been extensively tested for bugs and validated.

Unlike photoelectric and Compton interactions, coherent scattering is not always modelled in dedicated codes. Although coherent scattering can most often be neglected in SPET,[4] its contribution can be greater than 5% in high-Z detector materials such as bismuth germanate (BGO) at 250 keV and should thus be accounted for in PET simulations. Form factors should ideally be included in coherent and incoherent scattering cross-sections to best mimic the physics. In PET, the non-colinearity of the coincidence photons and the mean-free path of the positron should also be simulated as they induce some loss in spatial resolution. One of the major differences between codes lies in the modelling of the detector components. Ideally, interactions within the collimator (or septa in PET), crystal, light guide and photomultiplier tubes should all be simulated. In practice, simplified models are often used. In SPET, because modelling interactions within the collimator would be very inefficient (only about 1 out of 10000 photons goes through the collimator without interaction), most often, only the collimator geometric response is modelled analytically given the collimator characteristics (length, shape and size of the holes, thickness of the septa). This can cause inaccuracies for high energy photons (*i.e.* ^{131}I, high energy photons of ^{123}I) for which septal penetration and collimator scatter should not be neglected.[25] Analytical modelling of the collimator also disregards X-rays emitted after a photoelectric effect in the lead collimator which can significantly contribute to the energy spectra around 75 keV. In SPET, interactions within

the crystal are never modelled and the impact of the crystal, light guide and photomultiplier components upon the spatial resolution of the imaging device is modelled analytically instead, using an effective point spread function. For high energy photons however, it has been shown that a back-compartment whose parameters have to be empirically determined has to be modelled to better fit experimental data.[25] In dedicated PET simulators, the simulation of the detector components is usually more sophisticated than in SPET and most codes model interactions within the septa and the crystal.[19] However, these codes do not explicitly simulate the components located behind the crystal and also use analytical models to account for energy and spatial blurring caused by photomultipliers and associated electronics. In both SPET and PET, deadtime is not always accounted for, although it might be a large source of artefacts for acquisitions with high count rates. Validation studies and comparison with experimental data when possible are the only ways to characterise the accuracy of a code. As validation is both a major aspect of Monte Carlo simulations and the weakest point of most codes, a full section will be devoted to this issue.

The flexibility of the code depends on: 1) the types of source distributions that can be simulated; 2) the types of detectors that can be modelled; 3) the types of acquisition configurations that can be set up; 4) the types of output data that can be generated.

The source and attenuation distributions suitable for a Monte Carlo code can be based on geometrical or voxel representations. Geometry-based distributions are described using analytical functions in the three-dimensional (3D) reference space of the tomograph (*e.g.*, spheres, cylinders, parallelepipeds). The attenuation medium and radioactivity distribution within each geometric object are always assumed constant. This kind of source distribution can be used to represent simple phantoms or to approximate realistic activity distributions (*e.g.*, modelling brain, neck, thorax and legs with cylinders, lungs with ellipsoids).[27] Monte Carlo simulations using geometry-based distributions are very efficient since intersections between radiation path and source objects can be analytically calculated. However, the main limitation of geometric representations remains the poor adaptability to describe realistic clinical configurations. Recently, many efforts have thus been dedicated to the design of 3D anthropomorphic analytical phantoms reproducing in a very realistic way the shape and the composition of the human torso,[28] of the arms (axilla phantom [29]) and also including cardiac (MCAT phantom [30, 31]) and respiratory motions (NURBS phantom [32]). Such realistic distributions (including ribs, spine or lymph nodes) can indeed be described using complex mathematical functions. However, unlike analytical phantoms described only by simple geometric objects hence by few parameters, these complex analytical phantoms need many parameters to be described and are not necessarily advantageous from a storage point of view (compared to voxel-based phantoms). For instance, in the NURBS phantom, more than 200 parameters are needed just to describe the heart surface.

Voxel-based distributions are described by 3D voxel matrices. A radioactivity concentration and an attenuating medium are associated to each voxel. Voxel-based objects can thus be thought as volumes of radioactivity images and of attenuating media images. Some standard voxel-based anthropomorphic phantoms (*e.g.*, the Hoffman brain phantom,[33] the Zubal phantom,[34] the RSD™ phantom [35, 36]) are commonly used in Monte Carlo simulations for validating simulators or studying specific features (*e.g.*, scatter fraction). These anthropomorphic phantoms were obtained by segmentation of high resolution anatomical sections obtained from CT or MRI of patient studies or cadavers.[37] Typical voxel sizes are from few millimetre to few centimetre. Thanks to their fine and discrete representation, voxel-based distributions are well suited to model human anatomy. The possibility of using such voxel-based phantoms as an input of a Monte Carlo code is a prerequisite for simulating patient studies. However, this option is often not present in general purpose Monte Carlo codes, while some dedicated codes allow SPET and PET emission and transmission images of a clinical study to be directly used as maps of radioactivity and attenuation distributions.[22, 38] Such a facility allows pathological conditions or abnormalities in human organs to be easily simulated. The major advantage of the voxel-based phantoms is to allow easy simulations of very realistic clinical configurations. On the other hand, they are described at a fixed spatial resolution (only coarser sampling is possible) and restricted to a given anatomy.

Although both analytical and voxel-based anthropomorphic phantoms are becoming more and more sophisticated and can include very realistic attenuating media (obtained for instance from dosimetry measurements as mixtures of organic elements in dif-

TABLE I.—*Classification of the codes with respect to key features. Question marks mean that the piece of information was not found in published references.*

Parameters	General purpose codes				
	EGS4	MCNP	ITS	GEANT	SIMIND
Accuracy					
Interactions:					
—Photoelectric	Yes	Yes	Yes	Yes	Yes
—Compton scatter	Yes	Yes	Yes	Yes	Yes
—Coherent scatter	Yes	Yes	Yes	Yes	Yes
—Non-colinearity	Yes	Yes	Yes	Yes	—
—Positron range	Yes	Yes	Yes	Yes	—
Components:					
—Crystal	Yes	Yes	Yes	Yes	Yes
—Collimator	Yes	Yes	Yes	Yes	No
—Septa	Yes	Yes	Yes	Yes	No
—Dead time	No	?	?	No	Yes
Validation					
—Debugging	Yes	Yes	Yes	Yes	Partially
—Vs measurements	No	No in ET*	No in ET*	No	Partially
Flexibility					
Source:					
—Geometry based	Yes	Yes	Yes	Yes	Yes
—Voxel based	No	Not directly	?	No	Yes
—Patient images	No	No	?	No	Yes
Detectors:					
—Plane	Yes	Yes	Yes	Yes	Yes
—Ring	Yes	Yes	Yes	Yes	—
—Single-unit	Yes	Yes	Yes	Yes	—
—Block-unit	No	Yes	Yes	No	—
Configuration:					
—2D emission	No	Yes	Yes	No	Yes
—3D emission	No	Yes	Yes	No	—
—Transmission	No	Yes	Yes	No	Yes
—Dynamic studies	No	No	No	No	No
Data:					
—Energy spectra	Yes	Yes	Yes	Yes	Yes
—Sinograms	No	Yes	Yes	No	Yes
—Unscattered	Yes	Yes	Yes	Yes	Yes
—Scattered	Yes	Yes	Yes	Yes	Yes
—Randoms	No	Yes	Yes	No	—
—Singles	Yes	Yes	Yes	Yes	—
Efficiency:					—Geo
Approx. No	?		? No	Yes	
—Variance reduction	No	Yes	?	No	Yes
—Parallelization	No	Yes	?	No	No
Easy of use:					
—Familiar language	Fortran	Fortran 77+C	Fortran	C and C++	Fortran 90
—Public domain	Yes	Yes	Yes	Yes	Not really
—Docum./supp.	Yes	Yes	Partially	Yes	Yes

* ET: emission tomography.

ferent proportions,[39] accurate knowledge of the physiological distribution of different tracers is still needed. Modelling cardiac and respiratory motions is not necessarily enough: the dynamic processes of tracer uptake should ideally also be taken into account when simulating configurations that do not correspond to

Dedicated codes						
SPET only		PET only				SPET/PET
SIMSPECT	MCMATV	PETSIM	Reilhac	Eidolon	PET-EGS	SIMSET
Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yes	No	?	Yes	Yes	Yes	Yes
—	—	Yes	Analytically	No	Analytically	Yes
—	—	Yes	Yes	No	Analytically	Yes
No	No	Yes	Yes	Yes	Yes	Partially
Yes	No	—	—	—	—	Yes
Yes	No	Yes	Yes	Yes	Yes	Yes
No	No	Yes	No	No	No	No
Yes	Partially	Yes	Yes	Yes	Yes	Yes
Yes	Partially	Yes	Yes	Yes	Yes	Yes
Yes	Yes	Yes	No	Yes	Yes	Yes
No	No	No	Yes	Yes	Yes	Yes
No	No	No	Yes	Yes	Yes	No
Yes	Yes	No	No	Yes	Yes	Yes
—	—	Yes	Yes	Yes	Yes	Yes
—	—	Yes	No	No	Yes	Yes
—	—	Yes	Yes	Yes	Yes	No
Yes	Yes	Yes	Yes	Yes	No	Yes
—	—	?	Yes	Yes	Yes	Yes
No	No	?	Yes	No	No	Not directly
No	No	No	Yes	No	No	No
Yes	No	Yes	Yes	Yes	Yes	Yes
Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yes	Yes	Yes	Yes	Yes	Yes	Yes
—	—	Yes	Yes	No	Yes	No
—	—	Yes	No	No	Yes	Yes
Yes	Yes	No	Yes	Yes	No	No
Yes	Yes	No	No	No	No	Yes
Yes	Yes	No	No	Yes	No	No
Fortran and C	Fortran 77	Fortran	C	Objective-C	Fortran	C
Not really	Not really	From authors	From authors	Yes	From authors	From authors
Not really	Not really	From authors	Not yet	Yes	From authors	Yes

an equilibrium or for simulating dynamic studies without having to repeat as many Monte Carlo simulations as required by the time sampling of interest.

The types of detector that can be simulated are ring and plane detectors. The detector units can be large parallelepipeds, as for simulating SPET plane detec-

tors,[40, 41] or blocks of small parallelepipeds, appropriate to simulate the last generation PET multi-ring scanners.[42-46] The most flexible codes can also model detectors of more complex shapes, as ring arches, characterising new commercial PET systems based on large crystals.[47] Dedicated codes generally allow the number of detectors, size and composition, as well as the other geometrical and physical characteristics of the detection system, to be specified by the user in an input file or through a graphical interface. Such user-friendly detector specification is usually not directly supported by the general purpose codes, although configuring a new shape of detector is always possible, even if not straightforward with these codes. Most dedicated codes give a lot of choice for describing the detector. One of the most interesting component is the crystal, and usually BGO, NaI, Ge, CsF, LSO, GSO can be simulated.[48-52] With general purpose codes, the cross section data of every kind of detector medium can be calculated given the physical and chemical compositions of a material.

The flexibility of a code also depends on the types of acquisition configurations that can be modelled, for example the possibility of simulating PET tomographs in bidimensional (2D) and 3D assets, or to simulate SPET and PET transmission devices. Because these configurations are specific of SPET and PET systems, only dedicated codes can directly support them.

Also the variety of output data provided by the code has to be considered to assess the flexibility of the code. Whether energy spectra, projections or sinograms in 2D or 3D configurations, emission and transmission data, primary photons and scattered photons sorted by different scattering orders, randoms, single and coincident events in PET can be output is important for analysis and evaluation purpose.

The efficiency of the code mostly depends on the type of optimisation strategies adopted to increase the speed of simulations. Indeed, the major drawback of Monte Carlo methods is the high computation burden required to perform simulations with numbers of events representative of those involved in SPET and in PET.

Apart from programming virtuosity, the most common optimisation strategies concern: 1) analytical models of physical effects, allowing Monte Carlo simulation of some processes to be avoided while taking into account the resultant effects *a posteriori*, on the final response of the system; 2) approximations, based on geometrical considerations, in configuring tomographs and radioactive sources; 3) variance reduction techniques; 4) parallelisation techniques.

In most codes, analytical models of physical effects affecting energy and spatial resolution are present. Some examples of these analytical models have been discussed previously (like the collimator response model), because strictly affecting the accuracy of a code.

Geometrical approximations (*e.g.*, limiting the solid angle when generating an event or truncating the extent of the radioactive distributions nearby the tomograph edges) can be used to increase the efficiency in the collection of events.[53, 54] Indeed, only a small fraction of the total simulated events (<5%) are actually detected within the scanner field of view, causing simulations to be strongly ineffective. This kind of approximation can yield a reduction of a factor 5 in execution time.[53] For voxel-based distributions, for which radiation transport is more time consuming, segmentation procedures of attenuation distribution images [55, 56] or methods to optimize the computation of intersections between radiation path and voxels [57-59] can be used to decrease the computation time required by the discrete representation of the source object (by a factor close to 2). However, this kind of optimisation strategies, whose quoted examples represent only a small part of those presented in the literature, can affect the accuracy of simulations. Obviously, the code including the largest number of optimisation techniques is generally the most effective but not necessarily the most accurate. A potential Monte Carlo user must thus consider the kind of study of his interest before choosing the most appropriate code.

The name “variance reduction technique” derives from the fact that such techniques reduce the high variance of the few events detected by a measurement system when using conventional Monte Carlo methods involving analogue sampling.[4, 60] The scope of variance reduction techniques, also called non-analogue sampling, is “to force” the random choices so as to favour the events most likely to be detected. In SPET and PET, this is obtained by attaching a “weight” to each photon history, which represents the probability of that photon to follow a specific path or to undergo a particular interaction. In analogue sampling, weights are equal for all histories. In

non-analogue sampling, weights are low for histories that do not yield detectable photons and large for histories leading to detectable events. For example, photoelectric absorption is an undesirable effect because absorbed photons are not detected. Thus, variance reduction techniques assign a null weight to the sampling probability of photoelectric effect and only histories that do not involve absorption are simulated. As large weight variations should be avoided because they adversely affect the statistical properties of the simulated detected events, other techniques (like weight windows, particle splitting and Russian roulette) can be used to equalise the weights as much as possible. The effective gain in computation time resulting from the application of variance reduction techniques is a factor between 3 and 100 compared to analogue Monte Carlo methods. As the use of variance reduction techniques in SPET and PET can alter the statistical properties of the simulated data, such potential modifications should always be carefully studied when simulated data are used for assessing methods that deal with the statistical properties of the data (like statistical reconstruction algorithms).

With the advent of multi-processor computers, some codes were adapted to be implemented on parallel architecture,[20, 61, 62] yielding a reduction of computing time by a factor approximately equal to the number of used processors. The idea of parallelisation is to assign different instructions of the code to different processors working simultaneously.[63] Parallelisation is the only optimisation approach that does not interfere with the accuracy of the simulations, but specific programming languages and access to an appropriate multi-processor platform are required for the implementation.

Finally, the ease of use of a code is a function of: 1) the programming language and the supported platforms; 2) whether the code is in the public domain; 3) the availability of documentation and support.

In general purpose codes for which programming is always required, the programming language has to be considered as a factor affecting the ease of use. It is also better to be familiar with the programming language when planning to add or modify pieces of dedicated codes. The platforms on which the code runs can be an important parameter especially if running the code requires a lot of memory space or if efficient runs can only be achieved on machines with parallel architectures. Well-documented public domain codes can easily be shared and are more likely to be used by many and become part of the standard codes than non public domain codes. Documentation and support are key features determining the long-term existence and the future of a code.

In Table II, the main available Monte Carlo codes have been classified with respect to key features. The table is by no mean exhaustive in terms of Monte Carlo software or key features.

Validation of the codes

One of the most important issues related to the use of a Monte Carlo code is how the code has been validated. Obviously, the problem of validation is strictly connected with the problem of accuracy: only the results of thorough validation studies can warrant the accuracy of a code. The problem lies in defining "thorough" validation.

For both general purpose and dedicated Monte Carlo codes, validation deals at least with two aspects: 1) validation of the models for radiation emission, transport and interactions from the radioactive source to the measurement system; 2) debugging. In the case of dedicated codes or when a general purpose code is used for simulating PET or SPET configurations, there is a third important aspect: validation of the code with respect to the actual response of the measurement system, in our case, a tomograph. Here, we focus on this last aspect, since the others, although fundamental, do not fall properly under the competence of Nuclear Medicine and were already commented when discussing the accuracy of codes.

How well simulations can predict the physical response of the tomograph is usually checked by comparing the simulated and empirical values of some parameters, that can be experimentally measured and that characterise the physical performances of a tomograph. A simulator is then considered to be validated if it accurately reproduces the response of the experimental system. The parameters of interest that are used most often are the spatial resolution, scatter fractions, sensitivity, and count rates obtained in specific configurations, for instance, using the NEMA phantoms,[64] cylindrical phantoms, Utah phantom,[65] or anthropomorphic phantoms. These standard parameters have already been measured for some SPET [66] and PET scanners[67] (*e.g.*, Siemens/CTI ECAT[68], HR+[69], GE-Advance[70], Adac CPET[47]). Experimental and sim-

TABLE III.—*Classification of the codes with respect to validation.*

	Dedicated codes							
		SPET only			PET only			SPET/PET
	SIMIND	SIMSPECT	MCMATV	PETSIM	Reilhac	EIDOLON	PET-EGS	SIMSET
Parameters:								
—Resolution	No	Yes [14,15]	Yes [16,17]	Yes [18]	Yes [21]	Yes [20]	Yes [22]	Yes [75]
—Scatter fraction	Yes [13]	No	Yes [16]	Yes [18]	Yes [21]	Yes [20]	Yes [22]	No
—Sensitivity	No	Yes [15]	No	Yes [18]	No	Yes [20]	Yes [22]	No
—Count rate		No	No	No	Yes [18]	No	No	Yes [73]
No *Distributions:*								
—Energy spectra	Yes [13]	No	No	Yes [18]	No	Yes [20]	Yes [72]	No
—Sinograms	no	No	Yes [17]	No	Yes [21]	Yes [20]	Yes [22,72]	Yes [74,76]
—Noise properties	No	Yes [71]	No	No	No	No	Yes [73]	No
Images	No	Yes [14,15]	No	No	Yes [21]	Yes [20]	Yes [72]	Yes [76]
Data:								
—NEMA	No	No	No	No	No	Yes [20]	Yes [22]	No
—Utah	No	No	No	No	No	Yes [20]	No	No
—Anthropom.	No	No	No	Yes [29]	No	No	No	No
—Patients	No	No	No	No	Yes [21]	No	Yes [72]	No

No: not published to our knowledge.

ulated spectral and spatial distributions should also be compared to assess the accuracy of the simulations over the whole field of view.

Table III presents a classification of SPET and PET Monte Carlo codes with respect to validation. The features that have been validated are shown, as well as the bibliographic references reporting some validation results.

The very interpretation of validation results is often difficult. A statistical comparison of the numbers that correspond to the values of the parameter of interest requires a knowledge of the errors associated with these numbers. Because of the computational burden associated with Monte Carlo simulations, it is often difficult or even impossible to repeat the simulations several times in order to calculate both an average value and a standard deviation for each parameter of interest. When comparing energy and spatial distributions, a qualitative comparison based on visual inspection is often subjective. Again, a comparison based on statistical tests (*e.g.* χ^2 test) should be performed instead. Unfortunately, large statistical fluctuations usually affect simulated data due to the high computation time required for Monte Carlo simulations. Consequently, the power of relevant statistical tests is often low, making the result of statistical comparisons difficult to interpret.

Even when a code has been validated with regard to a large set of parameters, accuracy can never be warranted for all the possible uses of the code. The practical situation is often much worse: instead of validating the code with respect to a large set of parameters, validation is often performed in very specific configurations (for instance for ^{99m}Tc only in the 20% energy window) and with regard to few parameters only while the code is then used in much broader configurations (*e.g.*, involving other isotopes or a wider spectral range).

Which code for which purpose?

SPET and PET Monte Carlo simulations can be used for 5 types of application: 1) studying detector design (*e.g.*, collimator characteristics,[77] crystal,[78] detector geometry [8]; 2) analysing quantitation issues (*e.g.*, characterising the respective importance of scatter, attenuation, and partial volume effect [79]); 3) designing correction methods for quantitation;[73, 80, 81] 4) assessing the accuracy of quantitation methods (*e.g.*, tomographic reconstruction, scatter and attenuation correction [22, 82, 83]); 5) performing receiver operating characteristics (ROC) analyses.[84] Ideally, whatever the application, the code should be perfect in all respects. However, because there is no such thing as a perfect code, the code to be preferably used has to be chosen as a function of the application in two respects: first, it should be appropriate for simulating the configu-

rations needed for the application; second, the data produced by the code should be realistic with respect to the phenomena under study. The major resulting constraints for a given application are now detailed.

Studying detector design

Flexibility is a key property for a code to be appropriate for studying detector design. Another key property is the accuracy of the modelling of the detector components, especially those under study. In that respect, dedicated SPET simulators are often not well suited to that application, due to the lack of detailed simulation of the detector components. Finally, maintenance of the code is also quite important so that regular upgrades can be performed to follow the technological evolution of the detectors. Validation is a challenge when using Monte Carlo simulations for studying detector design. Indeed, the simulated configuration has usually no physical counterpart, and comparison of simulated and experimental data is impossible. A careful validation strategy has therefore to be developed to ensure that the simulated data accurately predict what would be obtained using the corresponding experimental device.

Analysing quantitation issues

For this application, the most important aspect probably lies in the definition of the simulated configuration, to ensure that it is realistic enough. For instance, errors in the predictions resulting from simulations can occur if cardiac or respiratory motions are ignored when defining the phantom, or if the simulated activity distribution is too simple. Hence, the type of possible input activity distributions is important, and efficient time modelling is a plus (*i.e.*, handling the time information instead of just repeating as many simulations as time points). Another issue with this application is that useful information can usually only be obtained if a representative range of configurations can be considered. For instance, to compare the impact of scatter in 2D and 3D PET, subjects with different size, morphology and activity distributions should be simulated. Efficiency of the code can therefore be a key feature to perform such studies.

Designing correction methods for quantitation

Patient-dependent Monte Carlo simulations can be used to identify unscattered, scattered and random events and select only the relevant components (basically primary photons and possibly very low angle scattered photons), providing corrections for scatter and random. Major problems with this correction approach are in defining *a priori* the patient-specific activity and attenuation distribution needed to run the simulation and to generate enough simulated data in a time compatible with a clinical use. For these reasons, both flexibility of the input activity and attenuation distributions (which should be voxel-based) and *efficiency* are key properties for a code to be appropriate for such application. Thanks to the fast progresses in computational power however, performing Monte Carlo based corrections for a clinical use is becoming a reality. Patient specific Monte Carlo simulations for correction purpose might become feasible in times compatible with clinical routine. The current time cost of employing a Monte Carlo scatter correction for a 3 bed position whole body PET study is the time needed for 1 extra 3D reconstruction (about 10 min for each bed position) plus about 4 min of Monte Carlo simulation.[54] The availability of Monte Carlo based correction methods on clinical scanners for evaluation purpose will tell soon the future role that Monte Carlo simulations can play in that context.

Assessing quantitation methods

An important point when using Monte Carlo simulations for assessing the accuracy of quantitation methods is to make sure that the characteristics of the data analysed by the quantitation method are realistic. *V*alidation of specific features is therefore crucial. For instance, to study the relevance of statistical reconstruction methods, care should be taken that the statistical properties of the simulated data are identical to those of experimental data (especially when using variance reduction techniques). When assessing scatter correction methods relying on energy information collected over a wide spectral range, the energy spectra of the simulated events should be identical to those that would be physically acquired. When assessing quantitation methods pertaining to a given isotope, the code should have been validated for this specific isotope first. Because unlike experimental data, simulated data almost never include imperfections related to the detection device (like a non-uniform response of the detector), the robustness of the quantitation methods with respect to such imperfections should be studied, to derive useful pre-

dictions regarding the performance of the quantitation methods on real data from those observed on simulated data.

ROC analysis

ROC analyses are used to characterise detection performance. In addition to human or mathematical observers, they require many images (typically hundreds) so that statistical analysis of the detection performance can be performed. Using Monte Carlo simulations in that context is therefore only feasible if efficient codes are available. Because such analyses are usually conducted to predict human observer performance in clinical situations, the type of possible input activity distributions is also crucial, in order to approach at best anthropomorphic configurations.

Monte Carlo codes: towards some standardisation?

Because all Monte Carlo codes present valuable features but also weaknesses, no code can be considered as a gold standard for SPET and PET simulations. Furthermore, it is often quite difficult to get precise descriptions of the features and performance of a specific code without going in details through the manual or even through the code, or without asking the author(s) directly. To help a potential user or developer to choose the code that is best appropriate for a specific application, there is therefore a need for a better standardisation of the description of the code features and of their performance.

The rationale for a standardisation of the description of the code features is that if such standardised description was available, a theoretical comparison of the codes would be made much easier. To achieve such a standardisation, all simulators should be described by specifying a list of precise characteristics, some of them are often not mentioned in the articles or manual pertaining to a code. Such a standardised description should include a precise definition of the components common to all codes (such as the random number generator and the sampling rules that are used) and obviously, a precise specification of all components that can make a code different from another and that have been listed in Section *What makes Monte Carlo codes different one from another*? By precise specification, we mean for example that the reference for the cross-section tables that are used should be given, or that the variance reduction techniques should be described. An important point that is often ignored in the description of a code is a list of the detector components or phenomena that are actually not modelled. Using a standardised description would facilitate the identification of the weak points of each code.

Because validation is of foremost importance for any simulation code and is currently the weakest point of most codes, we think that it should also obey some sort of standardisation. Similar to the standard procedures used for the quality control of a camera, standardised validation procedures would certainly help characterise the different codes, as at least comparable validation data would be available for different simulators. A validation standard should include test procedures demonstrating that the statistical properties of the simulated data are correct even when using variance reduction techniques. It should also include comparisons of simulated and experimental data when possible, corresponding to simple source geometry such as point or line sources, with and without scattering medium. Local and global energy spectra should be compared, together with point or line spread functions at different distances from the detector and in different energy windows. Comparison of simulated and experimental data obtained for more complicated phantoms (like anthropomorphic phantoms) should also be provided. Validation should be performed for each isotope. Standardised validation procedures should also include results regarding the computational efficiency of the codes. There is currently almost no way to compare the efficiency of different codes other than getting the codes and running them in identical configurations. Indeed, when specified, computing times are provided for different configurations simulated on different machines. If some typical configurations could be defined and run on a list of specific machines, the comparative assessment of the efficiency of different codes would be more straightforward. The task(s) to be performed should be defined in terms of the precise configurations (including object and detector descriptions) to be simulated, a number of counts to be detected, and some specifications of the hardware on which the code should be run (including machines with parallel processors). Results obtained in such circumstances should be

provided together with corresponding validation results, to combine the assessment of accuracy and computational performances.

Similar to other standardisation procedures, the definition of description and validation standards for Monte Carlo codes used in SPET and PET should obviously be the subject of specific documents approved by some recognised authorities. Because Monte Carlo codes are currently becoming an essential tool for SPET and PET quantification, we think that such standards should contribute to acknowledge the role of Monte Carlo simulations for SPET and PET quantitation.

Conclusions

Monte Carlo simulations are playing an increasing role in SPET and PET for protocol optimisation (from detector design to imaging parameters), evaluation of qualitative and quantitative accuracy of imaging protocols, and even as a base of patient-specific correction methods for increasing quantitative accuracy. While there is a number of general purpose and dedicated codes conveniently available for Monte Carlo simulations in SPET and PET, none of them can be currently considered as a standard. Having reviewed the specifics of the different codes, it appears that there is a definite need for a better standardisation of their feature description to facilitate their comparison. Some standardised validation studies are also strongly required to better characterise the performance of the different codes. These standardisation and validation efforts would certainly facilitate an efficient use of Monte Carlo simulation tools by the wide scientific community involved in SPET and PET research and practice. It would also contribute to definitely acknowledge the role of Monte Carlo simulations in SPET and PET so that the Monte Carlo methodology could become intimately bound to Nuclear Medicine imaging in a near future.

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