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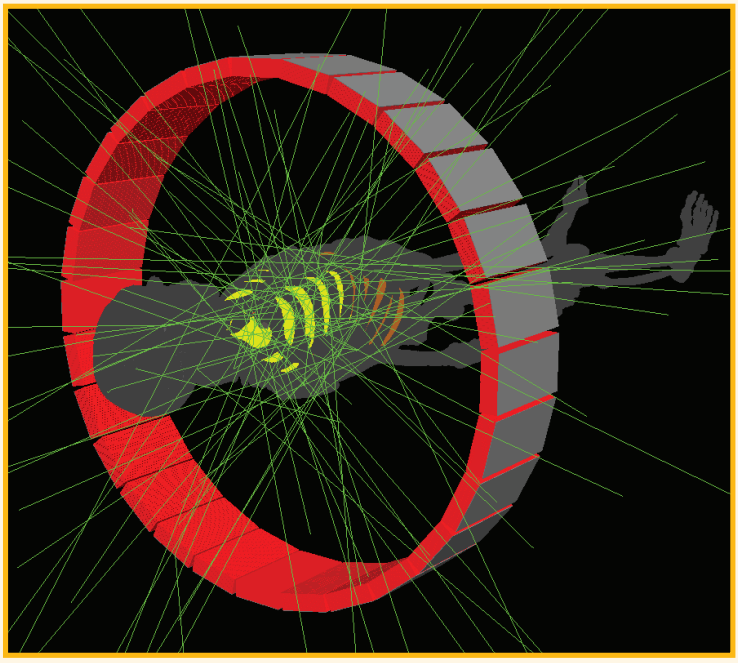

Edited by

Michael Ljungberg · Sven-Erik Strand · Michael A. King

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Monte Carlo Calculations in Nuclear Medicine

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Applications in Diagnostic Imaging

Michael Ljungberg
Lund University Hospital, Sweden

Sven-Erik Strand
Lund University Hospital, Sweden

Michael A. King
University of Massachusetts Medical School
Worchester, USA

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The IOMP website is being developed to include a scientific database of international standards in medical physics and a virtual education and resource center.

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Preface

Monte Carlo methods have become an important tool for exploring complicated systems and especially for investigation of imaging parameters in nuclear medicine. By using sampling methods based on probability distribution function in combination with methods that simulate the various particle interaction that can occur, a detailed radiation transport can be simulated from the patient into the imaging system. Monte Carlo simulation does not replace experimental measurements but offers a unique possibility to gain understanding in the underlying physics phenomena that form nuclear medicine images. It also provides a substantial help to researchers to develop methods for image improvement. When combining an accurate model of the imaging system and a realistic model of the patient's geometry and activity distribution, the simulated images can be highly clinically realistic and almost undistinguishable from a real patient measurement.

The first edition of this book was published in 1998. It was one of the first books that combined a description of the Monte Carlo methods and principles with relevant Monte Carlo programs and applications in the field of diagnostic nuclear medicine. It is now 14 years since that publication and we therefore felt that it was important to have a second edition since new and very powerful Monte Carlo programs and methods have become available.

This new edition provides the background to, and a summary of, the current Monte Carlo techniques that are in use today. The focus is still on the diagnostic imaging application but several programs that are described in the book also allow for charge-particle simulations applicable to dosimetry-related applications. The physics and technology behind scintillation camera imaging, SPECT/PET systems, and several MC simulation programs are described in detail. We have retained the aim from the first edition of the book, that is, to explain the Monte Carlo method and introduce the reader to some Monte Carlo software packages, developed and used by different research groups, and to give the reader a detailed idea of some possible applications of Monte Carlo in current research in SPECT and PET. Some of the chapters in the first edition of the book have been omitted to allow space for coverage of new programs and topics. Other chapters have been retained but updated. This does not mean that the chapters that we were not been able to include are unimportant; so thus a good suggestion is to have access to both editions.

Some chapters in this book describe in detail the physics and technology behind current simulated imaging detectors and systems in nuclear medicine and molecular imaging. The reason behind this is to let the reader be familiar with the imaging systems and to provide an understanding of the complexity of the systems that Monte Carlo programs are intended to simulate.

The editors are very happy that so many excellent authors were able to contribute to the present book and share their knowledge and experience in the field of Monte Carlo simulation and application. We would therefore like to thank all of them for their hard work and willingness to contribute to this book.

The text is intended to be useful both for education on graduate and undergraduate levels, and as a reference book on the Monte Carlo method in diagnostic nuclear medicine.

Editors

Michael Ljungberg is a professor at the Department of Medical Radiation Physics, Lund University, Sweden. He started his research in the Monte Carlo field in 1983 with a project involving simulation of whole-body counters, but changed focus to more general applications in nuclear medicine imaging and SPECT. As a parallel track to his development of the Monte Carlo code SIMIND, he started working in quantitative SPECT and problems related to attenuation and scatter in 1985. After completing his PhD at Lund University in 1990, he received a research assistant position at the department that allowed him to continue developing SIMIND for quantitative SPECT applications and establish successful collaborations with international research groups. In 1994, he became an associate professor and in 2005 a full professor. His current research also includes an extensive project in oncological nuclear medicine, where he develops dosimetry methods based on quantitative SPECT, Monte Carlo absorbed dose calculations, and registration methods, for accurate 3D dose planning for internal radionuclide therapy. He is also involved in the undergraduate education of medical physicists and supervises several PhD students. He is the deputy director of the Department of Medical Radiation Physics. In 2012, Dr. Ljungberg became a member of the European Association of Nuclear Medicines task group on dosimetry.

Sven-Erik Strand is a professor in medical radiation physics at Lund University. He received his Master of Science degree at the science faculty in 1972, his medical bachelor's degree at the medical faculty in 1981, and his PhD in 1979. At the University of Lund, he was before the director of undergraduate studies of the Department of Medical Radiation and presently he is the director of the Department of Medical Radiation. He has about 200 peer-reviewed publications and book chapters. Strand is a member in the steering group for creating the Lund University BioImaging Center (LBIC) and is now a member in its research board. He has been a member of several task groups in dosimetry and general nuclear medicine for the AAPM, ICRU, and the EANM task group, and recently, he has been a member of the EANM Radionuclide Therapy and Dosimetry Committee 2005–2011. He was awarded the SNM Loevinger–Berman Award for "Excellency in Radiation Dosimetry" in 2002.

Michael A. King received a BA in physics from the State University of New York at Oswego in 1969, and an MS in physics from the State University of New York at Albany in 1972. In 1978, he received his PhD in radiation biology and biophysics from the University of Rochester. From 1977 to 1979, Dr. King

was a postdoctoral fellow in medical physics at the University of Alabama Birmingham. In 1979, he joined the Department of Nuclear Medicine at the University of Massachusetts Medical School where he is currently professor of radiology, vice-chairman of radiology for research, and director of medical physics. He is certified by the American Board of Radiology in diagnostic radiological physics and medical nuclear physics. Dr. King is the author of over 160 peer-reviewed publications and the principal investigator of two current National Institutes of Health research grants. In 2006, he received the Ed Hoffman Memorial Award for "Outstanding Scientific Contributions to the Field of Computers and Instrumentation in Nuclear Medicine" from the Society of Nuclear Medicine. His areas of research interest include correction of SPECT studies for attenuation, scatter, and spatial resolution; detection and correction of patient motion; performance of human and numerical observer studies of lesion detection; quantification of activity; image registration; and image segmentation.

Contributors

Didier Benoit received his professional master's degree in optics and laser instrumentation in 2007 from Aix-Marseille University, France. In 2007, he entered the French CNRS (Centre National de la Recherche Scientifique) at CPPM (Centre de Physique de Particule de Marseille) in Marseilles and worked on the modeling, using the GATE Monte Carlo simulation tool, of a CT scanner developed by the imXgam group headed by Christian Morel, and on the optimization of CT system simulations in GATE. In 2009, he was hired as a GATE engineer by the IN2P3/CNRS (National Institute of Nuclear and Particle Physics) in Orsay (Paris Sud University) to assist GATE users, to integrate developments by GATE developers in new release of GATE, to maintain the OpenGATE website, and to manage the mailing list. Since 2010, he is also highly involved in developing iterative reconstruction algorithms for an original preclinical multimodular system of high resolution and high sensitivity dedicated to planar and SPECT imaging. His research is based on using GATE to characterize the imaging performance obtained using different original collimator design, and to optimize the reconstruction strategies.

Irène Buvat received her PhD degree in particle and nuclear physics from Paris Sud University, France in 1992. During her PhD work, she oriented her career toward applications of nuclear physics for medical imaging. She spent 1 year at the University College London, UK, working on single photon emission computed tomography (SPECT) and 2 years at the National Institutes of Health, Bethesda, USA, specializing in positron emission tomography (PET). In 1995, she entered the French Centre National de la Recherche Scientifique (CNRS) and is currently the head of a Quantification in Molecular Imaging team of the Imaging and Modelling in Neurobiology and Cancerology CNRS lab in Orsay, France. Her research activities focus on developing correction and tomographic reconstruction methods in PET and SPECT to improve the accuracy and reduce the variability of measurements made from PET and SPECT images. Her methodological approach is based on the use of Monte Carlo simulations to investigate all details of the forward imaging process so as to identify key aspects to be considered when developing quantification methods. She is currently the spokesperson of the worldwide OpenGATE collaboration developing the GATE Monte Carlo simulation tool dedicated to Monte Carlo simulations in emission and transmission tomography and radiotherapy. Irène Buvat is also largely involved in making quantification in SPECT and PET a clinical reality. She contributed to a number of studies demonstrating the clinical values of quantification to improve image interpretation, and obtained many research contracts with major companies in the field. She has authored and coauthored more than 90 peer-reviewed

articles. Irène Buvat teaches medical physics in several French Universities. She is an associate editor of *IEEE Transactions on Medical Imaging* and *IEEE Transactions on Nuclear Science* and serves on the editorial board of the *Journal of Nuclear Medicine* and on the international advisory board of *Physics in Medicine and Biology*.

Claude Comtat graduated in engineering physics at the EPFL in Lausanne, Switzerland in 1989. From 1990 to 1996, he was a teaching assistant at the Institute of High Energy Physics, University of Lausanne, Switzerland, where he earned a PhD in physics in 1996. From 1996 to 1998, he was a post-doctoral fellow at the PET Facility, University of Pittsburgh Medical Center. He is working since 1998 at the Service Hospitalier Frédéric Joliot (SHFJ), French Atomic Energy Commission (CEA). His research interests are in PET instrumentation, in particular statistical image reconstruction algorithms and analytical simulation tools.

Magnus Dahlbom received his BSc degree in physics from the University of Stockholm in 1982 and his PhD in medical physics from the University of California, Los Angeles in 1987. From 1987 to 1989, he was a research scholar at the Karolinska Institute in the Department of Radiation Physics. In 1989, he joined the faculty of the Department of Molecular and Medical Pharmacology at the University of California where he is now a professor. His interests are in nuclear medicine instrumentation, tomographic image reconstruction, and image processing. He has authored and coauthored more than 120 papers that have been published in scientific journals. Dr. Dahlbom is a member of the IEEE, the Society of Nuclear Medicine, and the AAPM.

Yuni K. Dewaraja received her BS in electrical engineering from the University of Western Australia in 1986 after which she worked for 2 years at the Atomic Energy Authority in Colombo, Sri Lanka. She received her MS in nuclear engineering from Kansas State University in 1990 and PhD in nuclear engineering from the University of Michigan in 1994. In 1996, she joined Dr. Kenneth Koral's group in the Division of Nuclear Medicine at the University of Michigan Medical Center where she is now an associate professor (Department of Radiology). Her current research interests include quantitative SPECT and patient-specific dosimetry in internal emitter therapy. Dr. Dewaraja is a member of the Society of Nuclear Medicine's Medical Internal Radiation Dose (MIRD) Committee.

Brian F. Elston is a senior computer specialist at the University of Washington. He received a BS degree in computer science from Western Washington University in 1999. After working as a game programmer and software engineer developing electron microscope control systems, he joined the Division of Nuclear Medicine at the University of Washington

in 2008. He is currently a member of the physics group in the Division of Nuclear Medicine. His professional interests include research in positron emission tomography (PET), simulation tools and studies, and software coding and algorithmic development. He is currently working on ASIM, an analytic simulator for PET, studies related to delta SUV measurements and assessing their impact on therapy in regard to disease classification as progression or regression, and comparative studies of display characteristics of various common vendor DICOM workstations used in the clinical practice of nuclear medicine.

Kjell Erlandsson was born in Stockholm, Sweden. He received his BSc and PhD (1996) in radiation physics at Lund University, Sweden. Since then, he has worked as a researcher at the Institute of Cancer Research, UK, Columbia University, USA, and the University College London, UK. His main interests are tomographic reconstruction, kinetic modeling, and partial volume correction for PET and SPECT. He is the author and coauthor of more than 60 peer-reviewed articles in the field of medical imaging.

Robert L. Harrison, PhD, is a research scientist at the University of Washington's Imaging Research Laboratory, Seattle. For more than 20 years, he has worked on the development and use of simulation for the study of emission tomography. He leads the development of SimSET (simulation system for emission tomography) and provides development support for the ASIM software (an analytic simulation of PET). With his colleagues at the University of Washington, he has used these simulations to characterize emission tomographs, prototype tomograph design changes, optimize clinical research studies, and design and test new image reconstruction algorithms and data corrections, resulting in important contributions in the areas of simulation efficiency, variance reduction, scatter and randoms correction, time-of-flight tomography, and tomograph optimization. His current research has two main foci: development of improved importance sampling for SimSET and using ASIM to understand how different sources of variability (e.g., coincidence counting noise, biologic variability, calibration error) affect PET measurements of response to therapy.

David R. Haynor, MD, is a neuroradiologist and professor of radiology at the University of Washington. His research interests range from GPU computing and image processing to bioinformatics.

Sébastien Jan graduated in fundamental physics in 1998, and obtained his PhD in nuclear physics from Joseph Fourier University, Grenoble, France in 2002. He joined the French Atomic Commission (CEA) in 2002 in a postdoctoral position, where he worked in the field of preclinical nuclear molecular imaging and Monte Carlo simulation. Since 2004, Dr. Jan has a CEA permanent research position and is leading a group in physics and image

processing for molecular imaging. He is the technical coordinator of the GATE Monte Carlo platform since 2003.

Paul Kinahan received his BSc and MSc in engineering physics from the University of British Columbia in 1985 and 1988, and his PhD in bioengineering from the University of Pennsylvania in 1994. He became an assistant professor of radiology and bioengineering at the University of Pittsburgh where he was a member of the group that developed the first PET/CT scanner in 1998. In 1997, he was awarded the IEEE-NPSS Young Investigator Medical Imaging Science Career Award. In 2001, he moved to the University of Washington in Seattle, where he is a professor of radiology, bioengineering, and electrical engineering and also the director of PET/CT physics at the University of Washington Medical Center. His work centers on the development and implementation of reconstruction algorithms for fully 3D PET scanners and the measurement of image quality. His research interests also include multimodality medical imaging, the use of statistical reconstruction methods, scanner optimization, and the use of quantitative analysis in PET oncology imaging. In 2011, he was appointed a fellow of the IEEE. He is a past president of the Society of Nuclear Medicine Computer and Instrumentation Council and the American Board of Science in Nuclear Medicine. He is a member of the Science Council of the American Association of Physicists in Medicine. He was the program chair of the 2002 IEEE NPSS Medical Imaging Conference (MIC), served twice on the Nuclear Medicine Imaging Steering Committee for MIC, and was the chair of the NMISC Awards Committee. He is an associate editor of *IEEE Transactions on Nuclear Science* and a member of the international advisory board for *Physics in Medicine and Biology*.

Kenneth F. Koral, PhD, became research professor emeritus at the University of Michigan, Ann Arbor in 2007 and received the Society of Nuclear Medicine's Loevinger–Berman Award in 2011. He has contributed chapters for three other books (*Nuclear Medical Physics*, Vol. 2, L Williams, ed., CRC Press, Inc., Boca Raton, Florida, 1987; *Therapeutic Applications of Monte Carlo Calculations in Nuclear Medicine*, H Zaidi and G Sgouros, eds., Institute of Physics Publishing, 2003; and *Quantitative Analysis of Nuclear Medicine Imaging*, H Zaidi, ed., Springer Science and Business Media, New York, 2005). He continues to publish with his colleague Dr. Yuni Dewaraja. He receives technical assistance from Charles Schneider and administrative assistance from Linda Brandt. He referees papers in nuclear medicine for various journals. In addition, he has taken up editing similar papers for a private company, TEXT Co. Ltd., which mainly has clients in Japan.

Erik Larsson received his PhD from Lund University in 2011, the topic of his thesis being the development of more realistic dosimetry models for internal dosimetry calculations in nuclear medicine. His research works include small-scale dosimetry models of mouse and rats and small-scale anatomic

dosimetry models of tissues with differentiated cell architecture. In these models, the Monte Carlo technique played an extensive part, with the main work performed with the MCNP codes. He now works part-time as a clinical medical physicist with the main objectives being labeling, quality control, administration, and dosimetry of radionuclide therapies, and part-time as a researcher at the Department of Medical Radiation Physics, Lund University, Sweden, where he is involved in the development of new dosimetry models.

Tom K. Lewellen is a professor of radiology and electrical engineering at the University of Washington. He received a BA in physics from Occidental College in 1967 and a PhD in experimental nuclear physics in 1972. After a postdoctoral fellowship designing beam optics for neutron therapy applications, he joined the Division of Nuclear Medicine at the University of Washington (UW) in 1974. Dr. Lewellen is currently the director of the physics group in the Division of Nuclear Medicine. His major research interests are positron emission tomography (PET) system development and improving methods for quantitative imaging (both in PET and in single photon emission tomography). The UW group is currently working on design and construction of new high-resolution animal PET scanners and MRI inserts, improved quantitative data corrections for PET/CT and SPECT/CT systems, faster Monte Carlo simulation software for emission tomographs, and new data analysis techniques for a wide variety of nuclear medicine studies.

Robert S. Miyaoka received a BS degree in general engineering from Harvey Mudd College in 1983. After briefly working for Hughes Aircraft Company, he went on to obtain his MS and PhD degrees in electrical engineering from the University of Washington in 1987 and 1992, respectively. He is currently a research associate professor in the Department of Radiology and an adjunct associate professor in the Department of Electrical Engineering at the University of Washington. He serves as the director of the Small Animal PET Imaging Resource and as the director of SPECT/CT Physics at the University of Washington. He has more than 20 years of experience in nuclear medicine instrumentation and physics research. His research has included time-of-flight PET and dual-head coincidence imaging. He also has developed a series of microcrystal element (MiCE) detectors for high-resolution PET imaging. His recent efforts have focused on PET detector designs that provide depth of interaction positioning and support multimodality imaging. His research interests also include preclinical PET imaging; multimodality PET/MR instrumentation development; and quantitative nuclear medicine and SPECT/CT imaging. Dr. Miyaoka has authored/coauthored more than 100 journal articles and conference proceedings.

Per Munck af Rosenschöld is the head of medical physics research at the Department of Radiation Oncology, Rigshospitalet, Copenhagen, Denmark. He received his MSc and PhD in radiation physics at Lund University,

Sweden in 1999 and 2003, respectively. During this work, he made extensive use of the Monte Carlo simulation code MCNP. He was a certified medical physics expert in Sweden and Denmark in 2009 and 2010, respectively. His research interest lay in radiation therapy with photon, proton/ions, and neutrons, focusing on methods for improving the precision of delivery, and optimizing dose distribution using radiobiological models and based on advanced CT, PET, and MR imaging. Since 2009, he is leading the medical physics and technology research at the Department of Radiation Oncology with a research group consisting of PhD students and postdocs in medical physics, radiation oncology, nuclear medicine radiology, biomedical engineering, and veterinary medicine.

Yoshihito Namito received a BS degree in nuclear engineering from Nagoya University in 1983 and an MS degree in nuclear engineering from the Tokyo Institute of Technology in 1985. He briefly worked for Ship Research Institute and stayed at the Radiation Physics Group of Stanford Linear Accelerator Center as a visiting scientist. He continued research while working at the National Laboratory for High Energy Physics to receive a PhD in engineering from the Tokyo Institute of Technology in 1995. He currently is an associate professor at Radiation Science Center in High Energy Accelerator Research Organization (KEK). He serves as a deputy manager of radiation control room in KEK. He has participated in the improvement of EGS4 code and the development of the EGS5 code for more than 20 years. His research interest also includes photon and electron transport in matter at an energy range of 1 keV to 1 TeV. He has also a long experience on experiment using synchrotron radiation. Dr. Namito has authored/coauthored more than 100 journal articles and conference proceedings.

Tomas Ohlsson received his radiation physics degree in 1985 and his PhD degree in 1996 (on positron emission tomography), both from the University of Lund, Sweden. In 1996, he became a research assistant at the Department of Radiation Physics, Lund. Since 1985, he has been working part time as a medical physicist in nuclear medicine. His interests are positron emission tomography, modeling in nuclear medicine, and dose planning for radionuclide therapy.

Mikael Peterson received his MSc in radiation physics in 2007 from the University of Lund. Since 2010, he has been a part-time PhD student at the Department of Medical Radiation Physics at Lund University, focusing on small-animal SPECT imaging. Since 2008, he has also been a part-time medical physicist at the Department of Radiation Physics, focusing on nuclear medicine—primarily in the area of radionuclide therapy.

W. Paul Segars is an associate professor of radiology and biomedical engineering and a member of the Carl E. Ravin Advanced Imaging Laboratories

(RAILabs) at Duke University, Durham, North Carolina. He received his PhD in biomedical engineering from the University of North Carolina in 2001. Dr. Segars is among the leaders in the development of simulation tools for medical imaging research where he has applied state-of-the-art computer graphics techniques to develop realistic anatomical and physiological models. Foremost among these are the extended 4D NURBS-based Cardiac-Torso (XCAT) phantom, a computational model for the human body, and the 4D Mouse Whole-Body (MOBY) and Rat Whole-Body (ROBY) phantoms, models for the laboratory mouse and rat, respectively. These phantoms are widely used to evaluate and improve imaging devices and techniques.

Scott J. Wilderman is a computations research specialist in the Department of Nuclear Engineering and Radiological Sciences at the University of Michigan. Since receiving his PhD in nuclear engineering from the University of Michigan in 1990, he has worked extensively on Monte Carlo modeling of radiation transport processes, with special focus in the modeling of electron and photon transport at energies below 1 MeV and more recently on dosimetry in radioimmunotherapy treatment. He has also been involved in the development of statistical image reconstruction methods for electronically collimated nuclear imaging cameras. Dr. Wilderman assisted in the development of the Monte Carlo radiotherapy dosimetry program DPM, which has since been modified extensively to permit patient-specific computation of dose to tumor and bone marrow in internal emitter radionuclide therapy. Dr. Wilderman was also one of the primary developers in the collaboration between the University of Michigan, the Stanford Linear Accelerator Center, and the High Energy Accelerator Research Organization (KEK) in Japan, which produced EGS5, a recent update of the extensively used EGS4 computer code system. In addition, Dr. Wilderman is the founder or cofounder of several companies involved in the U.S. fantasy baseball industry, and possesses unique experience and expertise in algorithms for evaluating and forecasting the performance of baseball players in the context of fantasy sports.

I. George Zubal received a bachelor degree in physics from the Ohio State University (OSU) (1972). He began his graduate work at OSU and focused on medical applications for his master's thesis (1974) in which he developed position-sensitive semiconductor detectors for nuclear medicine applications. He went abroad for his further studies and earned his PhD degree (1981) from the Universitaet des Saarlandes, Homburg, while developing Monte Carlo-based dosimetry maps overlaid onto CT images for therapy planning with fast neutrons at the German Cancer Research Center in Heidelberg, Germany. He returned to the United States to work as a postdoc in the medical department of the Brookhaven National Laboratories, Upton, New York. In 1984, he was recruited into industry (Picker International, Northford, CT) and worked as a senior scientist for nuclear medicine camera and computer

systems. He reentered the academic world in 1986 and became the technical director of the Section of Nuclear Medicine at Yale/New Haven Hospital and currently holds the position of associate professor in the Department of Diagnostic Imaging, Yale University School of Medicine. He has continued his work in Monte Carlo simulations of nuclear medicine patient geometries and has extended his image-processing techniques to evaluate functional disorders—notably for localizing seizures in the brains of epilepsy patients. While at Yale, he collaborated with Molecular NeuroImaging LLC, New Haven, on automated analyses for Parkinson's and Alzheimer's brain images since 2003, and transitioned to a full-time position at MNI in 2006.

1

Introduction to the Monte Carlo Method

Michael Ljungberg

CONTENTS

In the literature, we see today an increasing number of scientific papers which use Monte Carlo as the method of choice for the evaluation of a range of nuclear medicine topics such as the determination of scatter distributions, collimator design, and the effects of various parameters upon image quality. So what is the Monte Carlo method and why is it so commonly used as a tool for research and development?

A Monte Carlo method can be described as a statistical method that uses random numbers as a base to perform a simulation of specified situation. The name was chosen during the World War II Manhattan Project because of the close connection to games based on chance and because of the location of a very famous casino in Monte Carlo.

In most Monte Carlo applications, the physical process can be simulated directly. It only requires that the system and the physical processes can be modeled from known probability density functions (pdfs). If these pdfs can be defined accurately, the simulation can be made by random sampling from the pdfs. To obtain reasonable statistical errors, a large number of simulations of histories (e.g., photon or electron tracks) are necessary to get an accurate estimate of the parameters to be calculated.

Generally, simulation studies have several advantages over experimental studies. For any given model, it is very easy to change different parameters and investigate the effect of these changes on the performance of the system under investigation. Thus the optimization of an imaging system can be aided greatly by the use of simulations. A very early Monte Carlo study of the spectral distribution was made by Anger and Davis [1] that calculated the intrinsic efficiency and the intrinsic spatial resolution for NaI(Tl) crystals of different thicknesses and for various photon energies. Also, one can study the effects of parameters that cannot be measured experimentally. For example, it is impossible to measure the scatter component of radiation emitted from a distributed source independently of the unscattered component. By using a Monte Carlo technique incorporating the known physics of the scattering process, it is possible to simulate scatter events from the object and determine their effect on the final image. These studies have included measurements of the scatter to primary ratios, the shape of the scatter response function, the shape of the energy spectrum, proportion of photons undergoing various number of scattering events, and the effect attenuator shape and composition in addition to camera parameters such as energy resolution and window size. Hence, a simulation program can help the understanding of the underlying processes since all details of the simulation are accessible.

Overview papers of the Monte Carlo method and its applications in different fields of radiation physics have been given elsewhere by, for example, Raeside [2], Turner et al. [3], Andreo [4], and recently, Zaidi [5,6]. Here, we will outline only the basic methodology and how this may be applied to nuclear medicine problems.

Random Number Generator

A fundamental part of any Monte Carlo calculation is the random number generator. Basing the number on the detection of true random events, such as radioactive decay, the random number can be calculated but is generally very cumbersome and time consuming. On the other hand, true random numbers cannot be calculated since they, by definition, are randomly distributed and, as a consequence of this, they are unpredictable. However,

for practical considerations, a computer algorithm can be used to generate uniformly distributed random numbers from calculated seed numbers. An example of such an algorithm is the linear congruential algorithm where series of random numbers I_n are calculated from a first seed value I_0, according to the relationship

$$I_{n+1} = (aI_n + b) \bmod (2^k) \tag{1.1}$$

a and b are constants and k is the integer word size of the computer. If b is equal to zero, then the random number generator is called a multiplicative congruential random number generator. The following FORTRAN statement describes the random number generator in Equation 1.1. SEED is the initial value and RAN is the real random number in the range [0,1].

```
REAL FUNCTION RAN(SEED)
PARAMETER (IA=7141, IC=54773, IM=259200)
SEED = MOD(INT(SEED)*IA+IC,IM)
RAN = SEED/IM
END
```

It is important to realize that using the same value of SEED will give the same sequence of random numbers. Thus, when comparing different simulations, one needs to randomly change the initial value of SEED. This can be done, for example, by triggering a SEED value from a call to the system clock or by storing the value of the previous SEED immediately before exit of the previous simulation and then using this value as an initial value in the next simulation. This approach avoids obtaining the same results if a previous simulation is repeated. Repetition can in some cases be advantageous, for example, in a debugging procedure where small systematic errors can be difficult to spot if errors occur between simulations for statistical reasons.

An effect of this form of digital data representation in a computer is that there is a risk that the initial seed number can appear later in the random number sequence. If this occurs, then it is said that the random number generator has "looped." Although the following numbers are still randomly distributed, they are copies of the values generated earlier in the sequence. The severity of this effect depends on the application. The length of the sequence for the linear congruential generator is 2^k if b is odd. For the multiplicative congruential generator, the sequence length is $2^k - 2$. Other popular and high-quality random number generators are the RANMAR algorithm [7] and the RANLUX algorithm [8]. In the RANLUX algorithm, a user can define the level of accuracy ("luxury level") depending on the need. The lowest level provides a fast algorithm but the numbers may not pass some tests of uniformity. Higher levels move toward a complete randomness of the sequence.

Sampling Techniques

In all Monte Carlo calculations, some *a priori* information about the process to be simulated is needed. This information is usually expressed as probability distribution functions, pdfs, for different processes. For example, when simulating photon interactions, the differential cross-section data represent such information used to calculate the path length and interaction type. From this information, a random choice can be made on which type of interaction will occur or how far a photon will go before the next interaction. A probability distribution function is defined over the range of $[a,b]$. The function is ideally possible to integrate so that the function can be normalized by integration over its entire range. To obtain a stochastic variable that follows a particular probability distribution function, two different methods can be used.

Distribution Function Method

A cumulated cpdf(x) is constructed from the integral of pdf(x) over the interval $[a,x]$ according to

$$\text{cpdf}(x) = \int_a^x \text{pdf}(x')\,dx' \tag{1.2}$$

A random sample x is then sampled by replacing cpdf(x) in Equation (1.2) with a uniform distributed random number in the range of [0,1] and solved for x. Two examples of pdf(x)s and corresponding cpdf(x)s are shown in Figure 1.1.

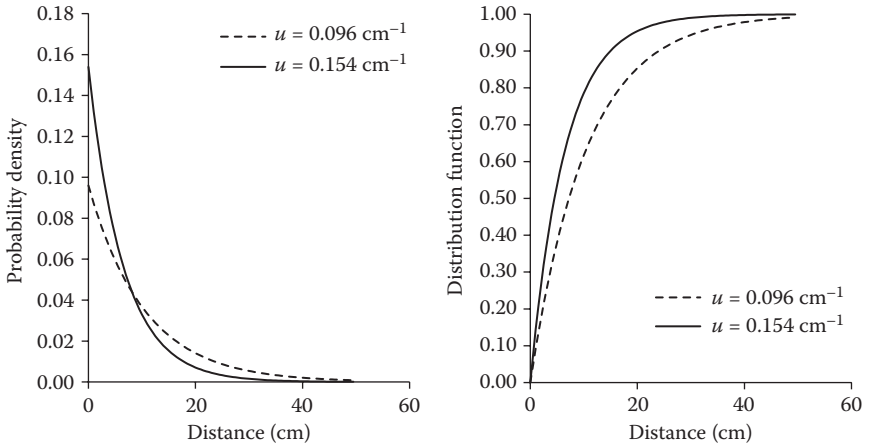

FIGURE 1.1
Two exponential probability distribution functions and their related calculated cumulated distribution function.

"Rejection" Method

Occasionally, the distribution function method is cumbersome to use due to mathematical difficulties in the calculation of the inverse of the cpdf. In these cases, one can use the rejection method that basically can be described by three steps.

Step 1: Let the probability distribution function, pdf(x), be bounded in the range [a,b]. Calculate a normalized function pdf*(x) = pdf(x)/max [pdf(x)] so the maximum value of pdf* is equal to unity.

Step 2: Sample a uniform distributed value of x within the range [a,b] from the relation $x = a + R_1 \cdot (b - a)$ and where R_1 is a random number.

Step 3: Let a second random number R_2 decide whether the sampled x should be accepted. This choice is made by calculating the function value of pdf*(x) from the sampled x value and then checked if $R_2 <$ pdf*(x). If this relation is fulfilled, then x is accepted as a proper distributed stochastic value. Otherwise, a new x value needs to be sampled, according to the procedure in Step 2.

"Mixed" Methods

A combination between the two methods, described so far, can be used to overcome potential problems in developing algorithms, based on either of the two methods alone. Here, the pdf(x) is the product of two probability distribution functions $\text{pdf}_A(x) \cdot \text{pdf}_B(x)$. The different steps in using this method are

Step 1: Let $\text{pdf}_A(x)$ be normalized so that the integral of $\text{pdf}_A(x)$ over the range [a,b] is unity.

Step 2: Let $\text{pdf}_B(x)$ be normalized so that the maximum value of $\text{pdf}_B(x)$ is equal to unity.

Step 3: Choose an x from $\text{pdf}_A(x)$ by using the distribution function method.

Step 4: Apply the rejection method on $\text{pdf}_B(x)$ using the sampled value x from Step 3 and check whether or not a random number **R** is less than $\text{pdf}_B(x)$. If not, then return to Step 3.

Sampling of Photon Interactions

Since this book will mainly focus on Monte Carlo applications for photon transport, describing the basic parts in simulating a photon path can be educative.

Cross-Section Data

Data on the scattering and absorption of photons are fundamental for all Monte Carlo calculations since the accuracy of the simulation depends on the accuracy in the probability functions, that is, the cross-section tables [9–11]. Photon cross sections for compounds can be obtained rather accurately (except at energies close to absorption edges) as a weighted sum of the cross sections for the different atomic constituents.

A convenient computer program developed to generate cross sections and attenuation coefficients for single elements as well as compounds and mixtures as needed is the XCOM [12]. This program calculates data for any element, compound, or mixture, at energies between 1 keV and 100 GeV. The program includes a database of cross sections for the elements. The total cross sections, attenuation coefficients, partial cross sections for incoherent scattering, coherent scattering, photoelectric absorption, and pair production in the field of the atomic nucleus and in the field of the atomic electrons are calculated. For compounds, the quantities tabulated are partial and total mass interaction coefficients, which are equal to the product of the corresponding cross sections and the number of target molecules per unit mass of the material. The sum of the interaction coefficients for the individual processes is equal to the total attenuation coefficient. A comprehensive database for all elements over a wide range of energies has been constructed by combining incoherent and coherent scattering cross sections from [13] and [14], photoelectric absorption from [15], and pair production cross sections from [16]. Figure 1.2a and 1.2b shows differential and total attenuation coefficients for H_2O and NaI, respectively. Note the discontinuity around 30 keV for NaI.

An aspect which deserves further attention is the fact that there exists a variation in the physical cross-section tables included in available Monte Carlo codes. This is of special importance when comparing results from different codes. The use of different cross-section data and approximations will usually yield different results and the accuracy of such results is not always obvious.

Photon Path Length

The path length of a photon must be calculated to decide if the photon escapes the volume of interest. Generally, this distance depends upon the photon energy and the material density and composition. The distribution function method can be used to sample the distributed photon path length x. If the probability function is given by

$$p(x)\,\mathrm{d}x = \mu \exp(-\mu x)\,\mathrm{d}x \tag{1.3}$$

Then the probability that a photon will travel the distance d or less is given by

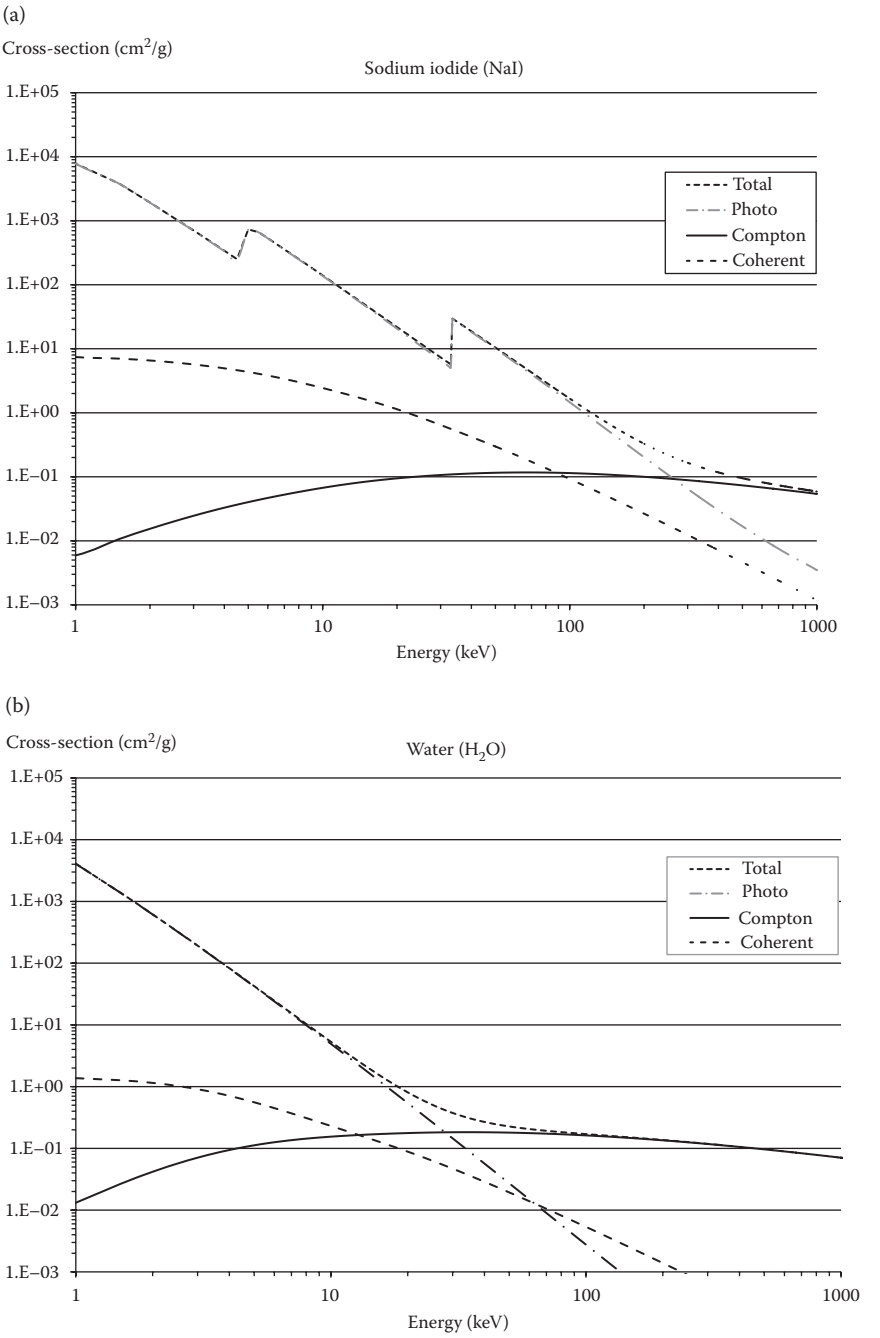

FIGURE 1.2
Distributions of total and differential attenuation coefficients, obtained from the XCOM program, for NaI (a) and H_2O (b).

$$\text{cpdf}(d) = \int_0^d \mu \exp(-\mu x)\,dx = [-\exp(-\mu x)]_0^d = 1 - \exp(-\mu d) \tag{1.4}$$

To sample the path length, a uniform random number R is substituted for $P(d)$ and the problem solved for d.

$$\left.\begin{aligned} R &= P(d) = 1 - \exp(-\mu d) \\ d &= -\frac{1}{\mu}\ln(1 - R) = -\frac{1}{\mu}\ln(R) \end{aligned}\right\} \tag{1.5}$$

Since $(1 - R)$ is also a random number and has the same distribution as R, one can simplify the calculation, according to (1.5).

Coordinate Calculations

After the sample of a new photon path length and direction, the Cartesian coordinate for the end point often is needed to be calculated to check if the photon has escaped the volume of interest. This can be made by a geometrical consideration where the new coordinate (x',y',z') in the Cartesian coordinate system is calculated from the photon path length and direction cosines, according to

$$\left.\begin{aligned} x' &= x + d \cdot u' \\ y' &= y + d \cdot v' \\ z' &= z + d \cdot w' \end{aligned}\right\} \tag{1.6}$$

where d is the distance between the previous point (x,y,z) and the new point of interest (x',y',z'). Assuming θ and ϕ are the polar and azimuthal angles in the Cartesian coordinate system and Θ and Φ is the polar and azimuthal angle defining the direction change, relative to the initial path of the photon, then the new direction cosines (u',v',w'), necessary to calculate the (x',y',z'), are calculated from

$$\left.\begin{aligned} u' &= \cos\theta \cdot u + \sin\theta[\cos\phi \cdot w \cdot u - \sin\theta\sin\phi \cdot v]/\sqrt{1 - w^2} \\ v' &= \cos\theta \cdot v + [\sin\theta\cos\phi \cdot w \cdot v + \sin\theta\sin\phi \cdot v]/\sqrt{1 - w^2} \\ w' &= \cos\theta \cdot w - \sin\theta\cos\phi \cdot \sqrt{1 - w^2} \end{aligned}\right\} \tag{1.7}$$

Selecting Type of Photon Interaction

The probability for a certain interaction type to occur is given by the differential attenuation coefficients. These are tabulated for different energies and materials. The sum of the differential attenuation coefficients for photoelectric effect (τ), Compton interaction (σ_{inc}), coherent interaction (σ_{coh}), and pair production (κ) is called the linear attenuation coefficient $\mu = \tau + \sigma_{inc} + \sigma_{coh} + \kappa$, or mass-attenuation coefficient if normalized by the density. To select a particular interaction type during the simulation, the distribution function method can be used. A uniform random number R is sampled and if the condition $R < \tau/\mu$ is true, then a photoelectric interaction will be simulated. If this condition is false, then the same value of R is used to test whether $R < (\tau + \sigma_{inc})/\mu$. If this is true, then one continues with a Compton interaction. If not, then the test $R < (\tau + \sigma_{inc} + \sigma_{coh})/\mu$ will determine if a coherent interaction has taken place. If all conditions are false, then a pair production is to be simulated. Obviously, this will only occur if the photon energy is >1.022 MeV.

Photo Absorption

In this process, the photon energy is completely absorbed by an orbital electron. In the simplest way, the photon history is terminated and the energy (and other parameters) is scored. However, it is possible that secondary characteristic x-rays and Auger electrons can be emitted. The relative probability for the two emissions is given by the fluorescence yield. If a characteristic x-ray is selected, then a new photon energy and an isotropic direction are sampled. The new photon is then followed until absorption or escape. Note the discontinuity in Figure 1.2. There are relatively large differences in attenuation coefficients close to these energies. Therefore, care should be taken so that the characteristic x-ray energy is properly set when sampling subsequent cross-section data. The deposit energy will be the incoming photon energy minus the binding energy for the rejected electron.

Incoherent Photon Scattering

Incoherent scattering, commonly denoted Compton scattering, means an interaction between an incoming photon and an atomic electron where the photon loses energy and changes direction. The energy of the scattered photon depends upon the initial photon energy, $h\nu$, and the scattering angle θ (relative to the incident path), according to

$$h\nu' = \frac{h\nu}{1 + (h\nu/m_o c^2)(1 - \cos\theta)} \tag{1.8}$$

where $h\nu'$ is the energy of the Compton scattered photon, m_o is the electron mass, and c is the speed of light in vacuum. One very commonly used method to sample the energy and direction of a Compton-scattered photon uses the algorithm developed by Kahn [17]. This algorithm is based on the Klein–Nishina cross-section equation:

$$d\sigma^{e}_{\gamma,\gamma e} = \frac{r_e^2}{2}\left(\frac{h\nu'}{h\nu}\right)^2\left(\frac{h\nu}{h\nu'} + \frac{h\nu'}{h\nu} - \sin^2\theta\right)d\Omega \tag{1.9}$$

The sampling method is based on a mixed method and is shown in the following Fortran statement:

```
ALPHA = HV / 511
TEST = (2*ALPHA+1)/(2*ALPHA + 9)
       RANDOM = 2*RAN(SEED)
IF(RAN(SEED).LT.TEST) THEN
       UU = 1+ALPHA*RANDOM
       IF(RAN(SEED).GT.4*(UU-1)/(UU*UU))GOTO 1
       COSTET = 1-RANDOM
ELSE
       UU = (2*ALPHA + 1)/(ALPHA*RANDOM+1)
       COSTET = 1-(UU-1)/ALPHA
       IF(RAN(SEED).GT.0.5*(COSTET*COSTET + (1/UU))) GOTO 1
ENDIF
```

The mathematical proof for the algorithm has been described by Raeside [2]. The rejection method, described earlier, is derived assuming scattering from a free electron at rest using the Klein–Nishina cross section. For situations where the incoming photon energy is the same order as the binding energy of the electron, the assumption of a free electron at rest becomes less justified. The cross section for this occurrence is given by

$$\frac{d\sigma_{\text{incoh}}}{d\Omega} = \frac{d\sigma_{KN}}{d\Omega}\cdot S(x,Z) \tag{1.10}$$

where $S(x,Z)$ is the incoherent scattering function [13], Z is the atomic number, and $x = (\sin(\theta)/2)/\lambda$ is the momentum transfer parameter that varies with the photon energy and scatter angle. It can be shown [18] that

$$\frac{d\sigma_{\text{incoh}}}{d\Omega} = \frac{d\sigma_{KN}}{d\Omega}\cdot\frac{S(x,Z)}{S_{\max}(x,Z)}\cdot K(h\nu,Z) \tag{1.11}$$

where $K(h\nu,Z)$ is constant for a fixed Z and energy. A scattering angle is sampled from Equation 1.8 using, for example, the Kahn's method. A momentum

transfer parameter, x, is then calculated and θ (obtained from the sampled x) is accepted only if a random number $R < [S(x,Z)/S_{\max}(x,Z)]$. Otherwise, a new scattering angle is sampled.

Coherent Photon Scattering

Coherent scattering is an interaction between an incoming photon and an electron where the direction of the photon is changed but without energy loss. This type of interaction leads to photons that are scattering mostly in the forward direction. The sampling technique for a coherent scattering is based on the Thomson cross section multiplied by the atomic form factor [13] $F(x, Z)$:

$$\frac{d\sigma}{d\Omega} = \frac{r_o^2}{2}(1 + \cos^2\theta)[F^2(x,Z)]d\theta d\varphi \tag{1.12}$$

It can be shown [18] that the probability of a photon being scattered into the interval dθ around θ is given by

$$P(\theta)d\theta = K(h\nu,Z) \cdot G(\theta) \cdot f(x^2,Z) \tag{1.13}$$

where $K(h\nu,Z)$ is constant for a fixed energy and atomic number, $G(\theta)$ has a fixed range and

$$f(x^2,Z) = \frac{F^2(x,Z)}{\int_0^{x^2_{\max}} F^2(x,Z)dx^2} \tag{1.14}$$

A value of x^2 is sampled from a precalculated distribution function of $f(x^2,Z)$. From this value, a scattering angle, θ, can be calculated provided that the relation $R < G(\theta)$ is fulfilled.

Pair Production

Simulating pair production is mainly a book-keeping procedure. An initial photon is assigned 511 keV and emitted in an isotropic direction. The location (x,y,z) and direction cosines (u,v,w) are stored and the photon is followed until absorption or escape. The current position is set to the annihilation location and a second 511 keV photon is emitted but in a direction opposite to the first and followed until absorption or escape. In some cases, there might be a need to simulate the effect of annihilation in flight—an effect that results in a non-180° emission between the two photons—and also account for the path length of the positrons.

Example of a Calculation Scheme

Figure 1.3 shows a flowchart of a photon simulation in a volume including photo absorption, incoherent, coherent scattering, pair production, and simulation of characteristic x-ray emission at the site of photo absorption.

Sampling of Electron Interactions

In many cases in Monte Carlo simulation of nuclear medicine applications and especially for imaging, the energy released by secondary electrons can be regarded as locally absorbed at the interaction site. However, there are some applications that this assumption does not hold. One example is absorbed dose calculations in small regions such as preclinical dosimetry [19]. Another example is the simulation of bremsstrahlung imaging where interacting electrons can produce photons required to be used for imaging [20–22]. In these applications, access to Monte Carlo codes that include a detailed charged particle simulation can be necessary.

A Monte Carlo simulation of charged particles, such as electrons and positrons, differs from a photon simulation in that most electrons interact by the weak Coulomb force which means that for each electron, history typically in the order of millions of interactions may occur before termination as compared to photons that undergo relatively few interactions (order of up to 10) before absorption. Most of the electron interactions will be inelastic scatterings with atomic electrons, which results in small angular deflections at each interaction site with a very small energy loss. Only a few of the electron interactions occur by elastic scattering with the atomic nuclei, production of secondary large-energy electrons, and bremsstrahlung photon generation. Inelastic electron interactions that result in a large change in kinetic energies and directions are sometimes called "catastrophic" events, whereas interactions resulting in only small changes in direction and energy are categorized as "noncatastrophic" events. Since noncatastrophic events will be in a vast majority, it becomes very time consuming to simulate the radiation transport in a detailed mode, that is, simulating each particle interaction explicit. Therefore, in order to reduce the calculation time, it is common to implement the so-called multiple-scattering methods where many electron interactions are condensed into larger steps (Figure 1.4).

The condensed history of electron transport was first suggested by Berger in 1963 [23] where he proposed simulation of the diffusion of electrons by a number of "snapshots" taken at different time or range intervals. The interactions between these snapshots were thus combined into "large"

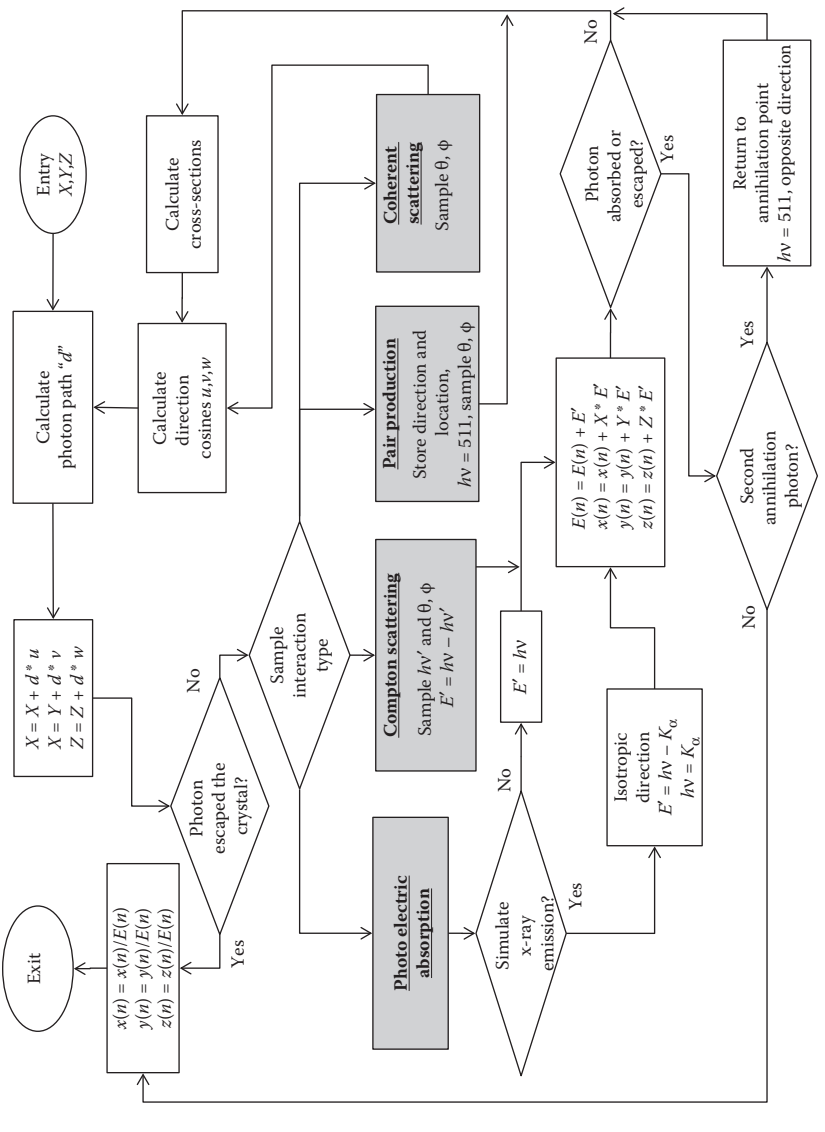

FIGURE 1.3
A flowchart describing the basic steps for simulation of photon transport in a defined volume.