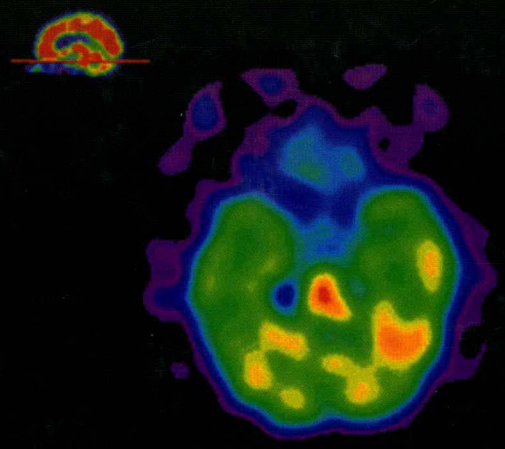

Functional Cerebral SPECT and PET Imaging

FOURTH EDITION

RONALD L. VAN HEERTUM
RONALD S. TIKOFSKY
MASANORI ICHISE

Wolters Kluwer Health | Lippincott Williams & Wilkins

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The authors dedicate this book to their wives,
Elyse Murphy (Van Heertum), Rita Tikofsky, and Eri Ichise,
and their children, Richard, Beth, Jonathan, and Kristin Van Heertum,
Lawrence Joseph Murphy III and Christopher Ryan Murphy;
Andrew Tikofsky and his daughter Shira Tikofsky; and Joshua Ichise.
The book is also dedicated to the memory of Melissa Jo Tikofsky.

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Preface

The five years following the publication of the third edition of *Functional Cerebral SPECT and PET Imaging* have experienced an almost exponential growth in the use of SPECT and PET functional brain imaging for clinical and research studies of neurologic and psychiatric disease states. Significant advances have been made in the area of receptor imaging using new tracers; new methods for quantifying imaging data are now more readily available to both clinicians and researchers. These changes compelled us to once again make significant changes to the third edition to provide our readers with reviews of the most recent applications of PET and SPECT so as to encourage their use in the clinical and laboratory setting.

This fourth edition of *Functional Cerebral SPECT and PET Imaging* has undergone a major expansion and reorganization. This edition is divided into three major sections. The first focuses on the basics of PET and SPECT imaging from the technical point of view. The chapters from the previous edition have been revised to take into account new developments in instrumentation and radiopharmaceuticals. There is a new chapter dedicated to PET radiopharmaceuticals and another dedicated to neuroreceptor imaging and kinetic modeling. The chapter on normal and correlative functional neuroanatomy has been divided into two chapters, one focusing on anatomy that includes PET/CT and the other discussing clinical findings and SPECT imaging. The second section is devoted to a discussion of the role of SPECT/PET in various clinical disease states. These chapters have undergone major revision. Not only are the chapters longer, but they also contain many illustrations to enhance the reader's understanding of current findings and issues relative to the disease state under discussion. The present edition has two chapters devoted to seizure disorders, one for SPECT and the other for PET. We have added separate chapters on psychiatric disorders, movement disorders, and addiction. The third section of this new edition is devoted to a gallery of clinical images grouped according to the disease states discussed in Section II. In addition, we included an introduction to this section, called "Helpful Hints," to guide those who are new to functional brain imaging in the interpretation of images they may encounter in the gallery and in their clinical and research practice. Included in the gallery are many "new" cases that expand the number of PET and PET/CT images.

It is our hope that this new edition will encourage clinicians and researchers to expand their use of SPECT and PET in their practice. We feel strongly that the future will see a greater integration of SPECT and PET imaging with other functional imaging modalities, such as fMRI, to increase our understanding of how the brain functions in health and disease. The next decade holds great promise for increased utilization and advances in this exciting field of medical imaging.

Ronald L. Van Heertum, M.D.
Ronald S. Tikofsky, Ph.D.
Masanori Ichise, M.D.

Preface to the Third Edition

In the few short years since the publication of the second edition of *Cerebral SPECT Imaging,* significant progress has occurred in the field of functional brain imaging. Most significant is the increased utilization of positron emission tomography (PET) in the clinical setting. There have also been significant advances in the areas of radiopharmaceutical development and instrumentation. In response to the rapid changes in brain imaging, we decided to change the scope (and, hence the title) of the book.

Cerebral SPECT and PET Imaging now has a new chapter pertaining to PET physics, instrumentation, and the basics of radiopharmaceuticals. The chapter on single photon emission tomography (SPECT) instrumentation, radiopharmaceuticals, and technical factors has been significantly revised. This chapter summarizes the current state of the field of clinical cerebral SPECT imaging. The entire book has been thoroughly revised and all of the clinical chapters have undergone critical review to reflect an appropriate balance between SPECT and PET applications. We have also expanded the presentation of clinical indications and case materials in all areas.

Many of the developments that were anticipated at the writing of the second edition of this atlas have now entered routine clinical practice. We look forward with great optimism to continued advances in the field of functional nuclear brain imaging particularly in the areas of receptor imaging, activation, and functional image analysis.

Ronald L. Van Heertum, M.D.
Ronald S. Tikofsky, Ph.D.

Acknowledgments

We would like to take this opportunity to acknowledge and express our sincere appreciation and thanks to our colleagues who have generously contributed chapters, case material, and critical reviews to this fourth edition of *Functional Cerebral SPECT and PET Imaging*. Our residents, in particular Dr. David K. Leung and Michal Kulon, deserve special thanks for helping to prepare the new cases that appear in the image gallery. Similar thanks go to members of our Nuclear Medicine technical staff (Ms. Irena Agrest and Mr. Lenhurst Leslie) and to Ms. Chitra Saxena, Ms. Lilya Deshenko, and the other members of the Columbia Kreitchman PET Center for locating and processing the cases used in this edition. In addition, special thanks go to Ms. Katherine Hickey and Ms. Nadia Rampersaud for their invaluable assistance in preparing the text and organizing the material that appears in the image gallery. This new edition could not have been possible without these contributions, both large and small. We offer our grateful thanks to them all.

No book makes it to publication without a good managing editor. We were fortunate to have such an editor in the person of Ryan Shaw of Lippincott Williams & Wilkins. His good natured prodding, prompting, and patience made it all come together in a timely fashion.

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CASES

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General Aspects of SPECT/PET Brain Imaging

1

SPECT Functional Brain Imaging: Instrumentation, Radiopharmaceuticals, and Technical Factors

Michael D. Devous, Sr.

INTRODUCTION

Functional brain imaging refers to that set of techniques used to derive images reflecting biochemical, physiologic, or electrical properties of the central nervous system (CNS). The most developed of these techniques are single-photon emission computed tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI). Of these, SPECT is the most widely available *and* widely applicable general measure of neuronal function. Some reviews may be of interest to the reader.[1-9] Although PET still provides the highest resolution tomographic images of brain function, modern SPECT images have similar resolution, making any differences relatively inconsequential in clinical application. Image resolution for fMRI is highly variable and technique dependent; for whole brain imaging it is generally not quite as good as PET or SPECT. Also, while the breadth of radiopharmaceuticals available for brain SPECT is not as great as that for PET, the number of SPECT tracers is expanding rapidly. SPECT perfusion tracers are FDA approved and available for wide distribution, whereas FDA approval for a nationally distributable PET tracer for brain function remains elusive (fluorine 18-labeled deoxyglucose [^{18}FDG] is approved for some applications, but brain function is not currently among them). The lack of a direct SPECT measure of metabolism remains a limitation. Because cerebral perfusion and metabolism are tightly coupled under most normal and pathologic circumstances, this difference may also be of no great clinical relevance.

This chapter provides an overview of the technical aspects of SPECT functional brain imaging, referring primarily to the most common SPECT brain function measure, regional cerebral blood flow (rCBF). SPECT images of rCBF are influenced by a number of factors separate from pathology, including (1) the quality of the tomographic device, (2) the radiopharmaceutical employed, (3) environmental conditions at the time of radiotracer administration, (4) characteristics of the subject (eg, age, gender, handedness), (5) the format used for image presentation, and (6) image processing techniques. All but the last aspect (6) are reviewed in this chapter. Image processing *per se* is not covered, because the considerable variety in the details of various methods (eg, filter choices, methods of reconstruction, attenuation, scatter correction schemes) is beyond the scope of this chapter. The reader is referred to available reviews.[3,10-14] However, the chapter contains a brief overview of the essential components of image processing necessary to produce high-quality SPECT brain images. In addition, an intercomparison of available techniques for the quantitative measurement of rCBF and a brief description of relevant radiation safety issues are provided. Finally, an introduction to SPECT brain imaging in molecular imaging and drug discovery and development is offered.

INSTRUMENTATION

Tremendous growth in SPECT instrumentation over the last two decades has resulted in commercially available, high-quality tomographs for SPECT brain imaging and sophisticated image processing hardware and software. SPECT instruments developed by university-based research paved the way for current devices, but industry has led the computational hardware development process. SPECT brain imaging is now a mature clinical entity, with stable commercial tomographs as well as cooperative ventures between academic centers and industry. Unfortunately, a low demand for brain-specific devices has led to the dominance of dual-head scanners that are ideal for cardiac SPECT. Not only has development of triple-head, or brain-only, cameras essentially stopped, it is no longer possible to even purchase a new triple-head SPECT camera. Nevertheless, they remain the best instruments for clinical SPECT scans. SPECT instruments fall into two categories: non–camera-based and camera-based systems, although the latter dominates both academic and commercial development.

Noncamera-Based Systems

Noncamera-based systems include rotating detector arrays, multidetector scanners, and fixed rings. Rotating detector array devices include the Tomomatic 2-, 3- and 5-slice machines (Medimatic, Inc) and the Hitachi three-head system. The Tomomatic's most characteristic attribute is the capacity for xenon 133 (^{133}Xe)-SPECT imaging, which requires very high sensitivity and rapid dynamic sampling (ie, complete tomographic studies every 10 seconds).[11,15] The advantage of ^{133}Xe SPECT is that it yields absolute quantitation of rCBF in mL/min/100 g tissue without arterial blood sampling. The Tomomatic, by changing collimators, can also produce moderate resolution (9–10 mm) rCBF images using iodine 123 (^{123}I)- or technetium-99m (^{99m}Tc)-labeled tracers. The Hitachi rotating detector array system is also capable of both ^{133}Xe and high-resolution (8–10 mm) static imaging.[16] Unfortunately, neither of these systems is still for sale.

The original fixed-detector research systems were the SPRINT,[17] the HEADTOME,[18] and the MUMPI.[19] They were designed with fixed detectors or a circular annulus of sodium iodide with an internally rotating collimator. The Shimadzu (HEADTOME) system, available only in Japan, is capable of high-sensitivity ^{133}Xe studies and moderate-resolution (10–12 mm) imaging using ^{123}I or ^{99m}Tc. The most widely available fixed-ring system is the CERASPECT,[20] first of the fixed sodium iodide annulus/rotating collimator machines to come to commercial production. It yields high-resolution images (8–10 mm), and is the only fixed-ring system still commercially available in the United States. In a recent reincarnation as the NeuroFOCUS system, it has demonstrated a 3-mm spatial resolution with ^{99m}Tc-labeled rCBF tracers in man, the highest spatial resolution SPECT or PET system that is commercially available (Fig. 1.1). Although resolution is excellent, image quality requires further development.

The original multidetector scanner, developed by Stoddart and colleagues[21] and later known as the Harvard multidetector scanner,[22] was commercially available from Strichman, Inc. This is a slice-based tomograph—as are the Hitachi, Shimadzu, and Tomomatic—but it is built with very thick crystals that operate much like pinhole cameras as they traverse through space to obtain tomographic data. Hill and colleagues[23] have demonstrated that this device can image ^{18}F in a single-photon (not PET) mode, as well as ^{99m}Tc and ^{123}I. It cannot perform ^{133}Xe SPECT.

Gamma Camera-Based Systems

Both single-head and multihead gamma camera-based systems are vastly more prevalent than dedicated tomographs, primarily because they can do both head and body SPECT. Multihead gamma camera-based systems have become so commonplace that previous concerns regarding limitations of the original systems (eg, poor head alignment, magnetic field aberrations, inadequate uniformity and linearity for tomography) are no longer even discussed in the literature. A few systems have also been designed to circumvent shoulders so that minimal radius scanning is possible. Most of these systems provide high-resolution images with static tracers (5–8 mm). Unfortunately, single-head systems suffer from poor sensitivity and prolonged imaging times.

A collaborative team from The University of Texas Southwestern Medical Center at Dallas and the nuclear engineering division of Technicare developed the first three-head gamma camera-based SPECT system to address the limited sensitivity of single-head systems.[24] This collaboration yielded a system capable of both head and body SPECT at high resolution with static tracers and with adequate sensitivity and rotation speed for dynamic tomography with ^{133}Xe. The first three-head system (PRISM) was installed in Dallas in late 1987 under the sponsorship of Ohio Imaging, now a division of Picker. Additional three-head SPECT instruments have been produced by Trionix (also as a by-product of the collaboration mentioned above), Toshiba, General Electric, and Siemens. Three-head SPECT systems currently are the most sophisticated instruments for brain SPECT (Fig. 1.2). There are more than 1000 such units installed, indicating wide acceptance of this technology. The first ^{133}Xe SPECT images in humans from a three-head system (PRISM) were produced in late 1992 by the Dallas group (Fig. 1.3) and have also been produced by Toshiba. Unfortunately, no manufacturers currently offer triple-head gamma cameras, although refurbished units are periodically available.

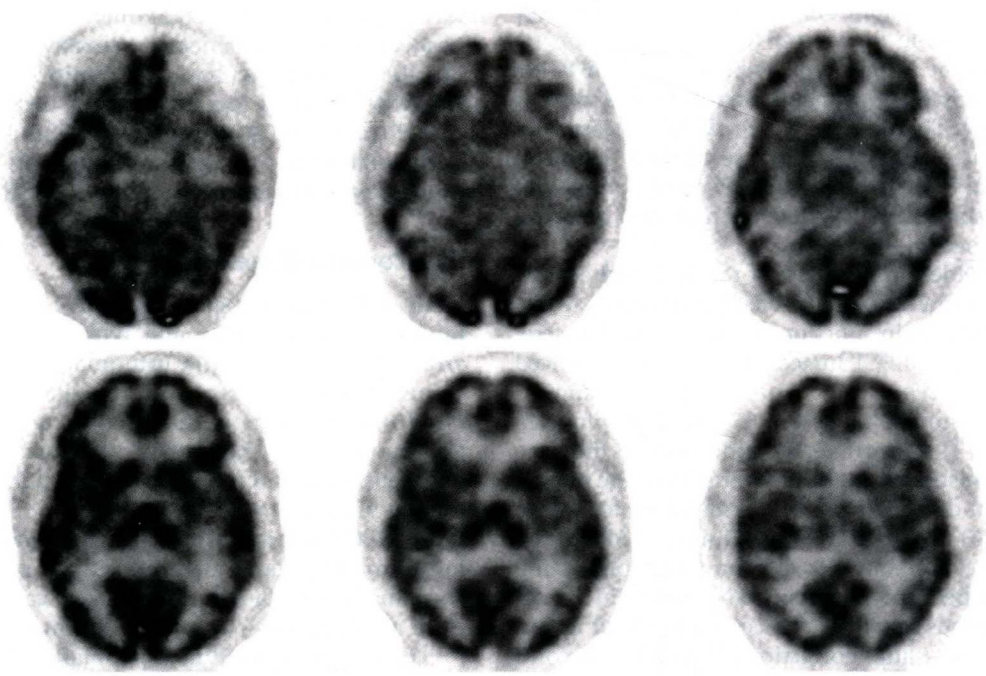

Figure 1.1. High-resolution rCBF images from a healthy control with the NeuroFOCUS High-Definition Focusing Emission Tomographic Scanner (HDFET) using ^{99m}Tc-HMPAO. (Images provided courtesy of NeuroPhysics Corp.).

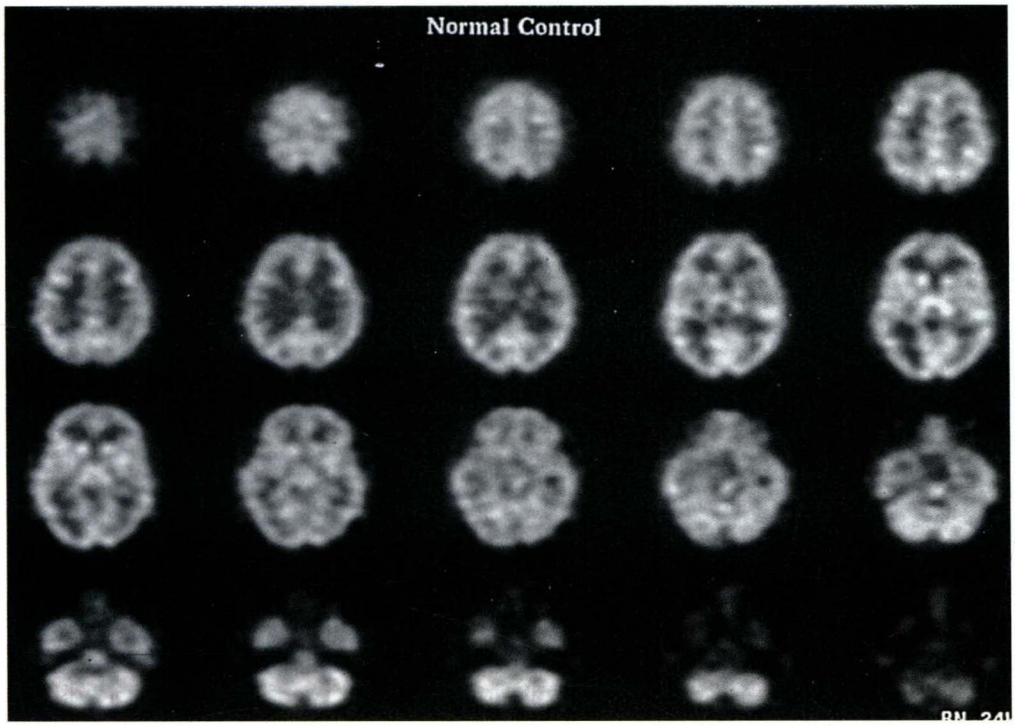

Figure 1.2. Typical high-resolution rCBF SPECT images obtained using ^{99m}Tc-HMPAO and the PRISM 3000S tomograph in a normal volunteer.

Image-Processing Essentials

State-of-the-art SPECT systems can be expected to provide high-resolution imaging of statically distributed brain radiopharmaceuticals with patient imaging times of 10–20 minutes (see Figs. 1.1 and 1.2). All of the currently available three-head systems offer excellent spatial resolution: 6-mm resolution in the cortex and about 7 mm at the center of the brain, with appropriate collimators and ^{99m}Tc-hexamethylpropyleneamine-oxime (HMPAO) (exametazime or Ceretec, GE Healthcare) or ^{99m}Tc-ethyl cysteinate dimer (ECD) (bicisate or Neurolite, Bristol-Myers Squibb Medical Imaging).

To achieve such resolution, a few simple principles should be followed. First, it is necessary to reconstruct nearly motion-free data. A key instrumentation feature to facilitate collection of motion-free data is the capability of sequential image acquisitions. That is, it should be possible to acquire multiple short studies back to back and subsequently discard segments degraded by patient motion (eg, collecting five 4-minute studies to achieve a 20 minutes total acquisition time).

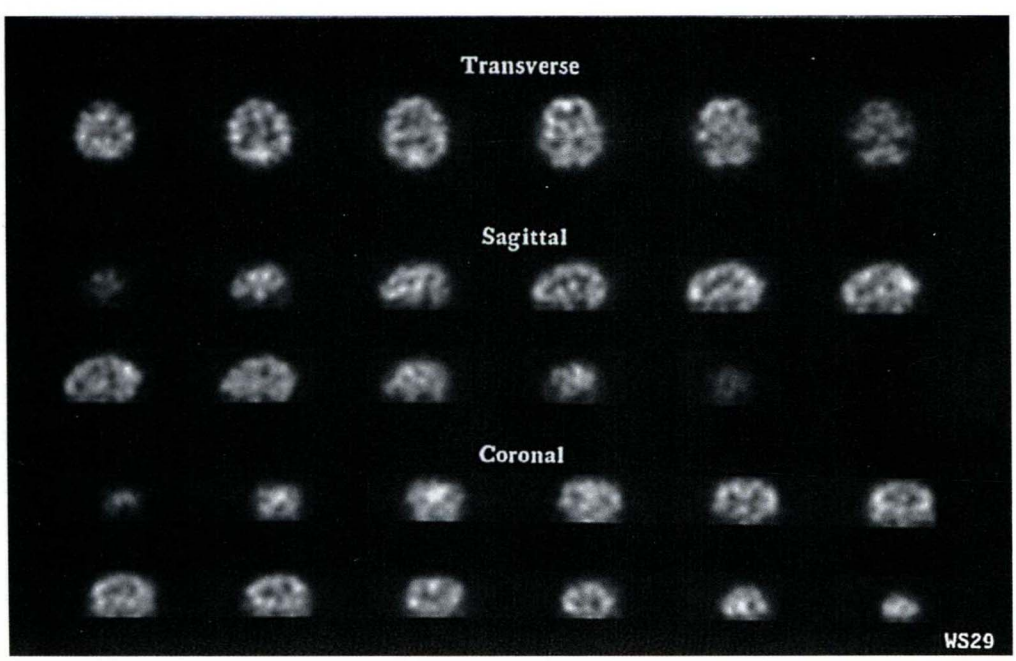

Figure 1.3. Quantitative (mL/min/100 g) dynamic rCBF images obtained using ^{133}Xe and the PRISM 3000S. Images were obtained in 4 minutes, including 1 minute of washin and 3 minutes of washout of the inert gas tracer.