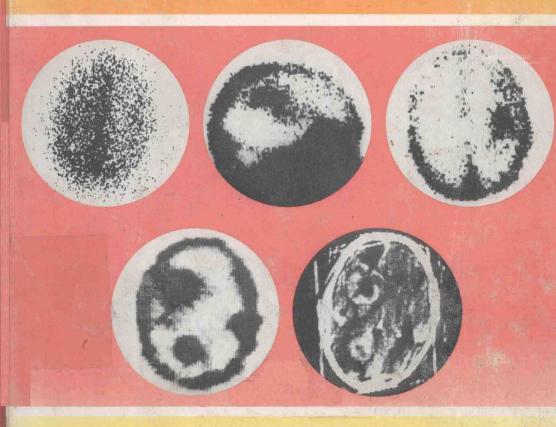
## NONINVASIVE BRAIN IMAGING

COMPUTED TOMOGRAPHY AND RADIONUCLIDES



HAROLD J. DeBLANC, JR.
JAMES A. SORENSON

# Noninvasive Brain Imaging:

### Computed Tomography and Radionuclides

#### Edited by

Harold J. DeBlanc, Jr., M.D.

Director, Nuclear Medicine
University of Utah

James A. Sorenson, Ph.D.

Director, Medical Physics
University of Utah

Distributed by
Publishing Sciences Group, Inc.
162 Great Road
Acton, Massachusetts 01720

ISBN 0-88416-137-4

This book is protected by copyright. No part of it may be reproduced in any manner without the written permission of the publisher.

<sup>© 1975</sup> by The Society of Nuclear Medicine, Inc. Library of Congress Number 75-27242 Printed in the United States of America All rights reserved

# Noninvasive Brain Imaging:

Computed Tomography and Radionuclides

#### Series Editor

Monte Blau, Ph.D.
State University of New York at Buffalo
Buffalo, New York

#### Review Board

Trevor D. Cradduck, Ph.D.

Toronto General Hospital

Toronto, Ontario, Canada

Donald E. Wood, M.D.
Ontario Medical Association
Toronto, Ontario, Canada

# This volume is affectionately dedicated to Georgie and Lucy

#### **Participants**

#### Philip Braunstein

New York University Medical Center New York, New York

#### Thomas F. Budinger

University of California Berkeley, California

#### R. Edward Coleman

Washington University School of Medicine Mallinkrodt Institute of Radiology St. Louis, Missouri

#### Ernest W. Fordham

Rush-Presbyterian, St. Luke's Medical Center Chicago, Illinois

#### John C. Harbert

Georgetown University Medical Center Washington, D.C.

#### Paul B. Hoffer

University of California, San Francisco San Francisco, California

#### David E. Kuhl

Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

#### William H. Oldendorf

University of California School of Medicine Los Angeles, California

#### Anthony M. Passalaqua

New York University Medical Center New York, New York

#### Michael E. Phelps

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Henry N. Wagner, Jr.

The Johns Hopkins Medical Institutions Baltimore, Maryland

#### Michael J. Welch

Washington University School of Medicine

Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Contributors

#### Abass Alavi

Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

#### Philip O. Alderson

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Stewart P. Axelbaum

Georgetown University Medical Center Washington, D.C.

#### John J. Bouz

Foothills Hospital Calgary, Alberta, Canada

#### Norman E. Chase

New York University Medical Center New York, New York

#### Frank H. DeLand

University of Kentucky Medical Center Lexington, Kentucky

#### Giovanni DiChiro

NINDS, National Institutes of Health Washington, D.C.

#### Hector E. Duggan

Foothills Hospital Calgary, Alberta, Canada

#### Roy Q. Edwards

Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

#### John O. Eichling

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Craig A. Fenton

Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

#### Mokhtar Gado

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Randolph O. George

The Johns Hopkins Medical Institutions Baltimore, Maryland

#### Edward J. Hoffman

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Bernard Hoop, Jr.

Massachusetts General Hospital Boston, Massachusetts

#### Irvin I. Kricheff

New York University Medical Center New York, New York

#### William T. McLaughlin

Santa Clara Valley Medical Center San Jose, California

#### Nizar A. Mullani

Washington University School of Medicine St. Louis, Missouri

#### Thomas P. Naidich

New York University Medical Center New York, New York

#### Marcus E. Raichle

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Martin M. Reivich

Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

#### Dieter Schellinger

Georgetown University Medical Center Washington, D.C.

#### Maria G. Straatmann

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### Michel M. Ter-Pogossian

Washington University School of Medicine Mallinckrodt Institute of Radiology St. Louis, Missouri

#### David A. Turner

Rush-Presbyterian, St. Luke's Medical Center Chicago, Illinois

#### Paul M. Weber

Kaiser-Permanente Medical Center Oakland, California

#### Robert A. Zimmerman

Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

### Contents

Participants and Contributors vi

1	Foreword
3	<ol> <li>Ten Years of Brain Tumor Scanning at Johns Hopkins: 1962–1972 Randolph O. George and Henry N. Wagner, Jr.</li> </ol>
17	2. Molecular Criteria for Blood-Brain Barrier Penetration William H. Oldendorf
25	3. New Short-Lived Radiopharmaceuticals for CNS Studies  Michael J. Welch, John O. Eichling, Maria G. Straatmann,  Marcus E. Raichle, and Michel M. Ter-Pogossian
45	4. Dynamic Time-Dependent Analysis and Static Three-Dimensional Imaging Procedures for Computer-Assisted CNS Studies  Thomas F. Budinger, Frank H. DeLand, Hector E. Duggan, John J. Bouz, Bernard Hoop, Jr., William T. McLaughlin, and Paul M. Weber
67	5. Computerized Emission Transaxial Tomography and Determination of Local Brain Function David E. Kuhl, Abass Alavi, Martin Reivich, Roy Q. Edwards, Craig A. Fenton, and Robert A. Zimmerman
81	6. Tomographic Radionuclide Brain Imaging with the Anger Tomoscanner Ernest W. Fordham and David A. Turner

87	7. Transaxial Emission Reconstruction Tomography: Coincidence Detection of Positron-Emitting Radionuclides Michael E. Phelps, Edward J. Hoffman, Nizar A. Mullani, and Michael M. Ter-Pogossian
111	8. Computerized Transaxial Transmission Reconstruction Tomography Michael E. Phelps, Edward J. Hoffman, Mokhtar Gado, and Michel M. Ter-Pogossian
147	9. Clinical Comparison of Radionuclide Brain Imaging and Computerized Transmission Tomography, I Mokhtar Gado, R. Edward Coleman, and Philip O. Alderson
173	10. Clinical Comparison of Radionuclide Brain Imaging and Computerized Transmission Tomography, II Anthony M. Passalaqua, Philip Braunstein, Irvin I. Kricheff, Thomas P. Naidich, and Norman E. Chase
183	11. A Preliminary Comparison Between ACTA Scans and Radionuclide Imaging Studies of the Central Nervous System John C. Harbert, Stewart P. Axelbaum, Dieter Schellinger, and Giovanni DiChiro
195	12. The Past, Present, and Future of Noninvasive Brain Imaging: Panel Discussion Paul B. Hoffer, Philip Braunstein, Thomas F. Budinger, R. Edward Coleman, Ernest W. Fordham, John C. Harbert, David E. Kuhl, William H. Oldendorf, Michael E. Phelps,

Henry N. Wagner, Jr., Michael J. Welch

of

Index 209

### **Foreword**

or the past 10 years radionuclide imaging of the brain has provided a reliable and useful technique for the diagnosis of brain disease. The low cost and noninvasive nature of the procedure has made it the screening test of choice for brain disease. The role of radionuclide brain imaging has recently been challenged, however, by the development of a new transmission scanning technique, computerized transaxial tomography, or CTT scanning.

Seldom has a new diagnostic technique received such rapid acceptance as CTT scanning. It has been suggested that this may have a profound impact on the routine use of radionuclide brain imaging. It is therefore desirable at this time to examine the roles of these two techniques in the diagnosis of brain disease and to evaluate the potential for future developments. This book presents such an assessment by several leading experts in the field.

The first two chapters are devoted to the present status of radionuclide brain imaging and to current concepts of the blood-brain barrier and its importance in radionuclide studies, particularly in regard to the development of new radiopharmaceuticals for brain imaging. The next five chapters discuss other new concepts and potential future developments. These include the use of new radiopharmaceuticals, especially those containing cyclotron-produced radionuclides, including 11C, 13N, and 15O. The desirable decay characteristics of these radionuclides and their importance as labels for physiological compounds have long been recognized. The technology for labeling these compounds has been demonstrated. What remains to be done is to develop relatively inexpensive methods for producing them in a clinical environment. It should be noted that the cost of the currently available compact cyclotron even now is not too different from that of a single CTT scanner, and there is potential for the development of a lower cost, smaller, medical cyclotron more suitable for routine clinical use.

Computerized reconstruction tomography in brain imaging is not, of course, new or unique to transmission techniques since it was introduced by Kuhl and coworkers in nuclear medicine over 10 years ago. The work of these investigators in the development of computerized radionuclide transaxial tomography, or CRTT scanning,

Foreword | 1

summarized in Chapter 5, is particularly worthy of review at this time. Also presented in other chapters are descriptions of techniques and early clinical results for reconstruction tomography employing the scintillation camera and a new imaging device for positron emitters. The latter is of particular importance with respect to the cyclotron-produced radionuclides mentioned earlier. It is possible that, by providing improved images and new tests using new radiopharmaceuticals, CRTT imaging could have as great an impact as CTT scanning on the diagnosis of brain disease.

The last five chapters are devoted to CTT and radionuclide scanning, including comparisons of clinical results obtained by both procedures. Chapter 8 presents an especially useful and comprehensive analysis of the capabilities and limitations of current CTT scanners as well as a discussion of their potential for further improvements. The final chapter presents a panel discussion among a variety of experts in radionuclide and CTT scanning.

It is expected that other noninvasive brain-imaging techniques besides those discussed here may also be developed further in the next few years. One of these, for example, is the use of improved diagnostic ultrasound techniques. While their potential is recognized, however, a discussion of these techniques was considered beyond the scope of this book.

We are grateful to Dr. Monte Blau for his support and assistance in the careful review of this work and to Margaret Glos and Christa Foster of the Society of Nuclear Medicine for their help in the organization of the symposium given in Salt Lake City and for their continued assistance throughout the publication of this volume. We are also indebted to Margaret Ann Bowman for her patient and diligent performance in the extensive task of preparing the typewritten manuscripts. Finally, we would like to thank the authors for their promptness in reviewing and returning the edited manuscripts, which helped to make rapid publication of this book possible.

HAROLD J. DEBLANC, JR. JAMES A. SORENSON

### Ten Years of Brain Tumor Scanning at Johns Hopkins: 1962-1972

Randolph O. George and Henry N. Wagner, Jr.

The enormous technological advances that we are observing today in the fields of diagnostic radiology and nuclear medicine, particularly in relation to the study of brain disease, suggest that it may be worthwhile to review our past experience to gain insight into possible future developments. In this chapter we will review our experiences in brain tumor scanning over the past 10 years at the Johns Hopkins Hospital. Included in our discussion will be changes in technology that have occurred, the relationship of brain scanning to other diagnostic procedures in patients with neurological disease, the sensitivity of brain scanning for the detection of tumors, the effect of various diagnostic procedures on the interval between onset of symptoms and time of surgery for brain tumors, and changes in the operative mortality and 2-year survival of patients with a variety of brain tumors.

#### Materials and Methods

During the period from January 1, 1962, to May 1, 1972, 1,050 patients with the diagnosis of "brain tumor" were seen at the Johns Hopkins Hospital. The subjects selected for this study included only those among this group meeting the following additional criteria: (A) intracranial brain tumor confirmed by tissue diagnosis; (B) brain scans performed within 1 year preceding the diagnosis; and (c) all other neurological procedures performed at the Johns Hopkins Hospital. Of the 1,050 patients, 369 (35%) met all of the criteria prescribed for inclusion in this study.

The relative sensitivities of brain scans, arteriograms, and air studies for all tumors were examined with regard to tumor location and type of tumor. Types of tumor were divided into four groups: meningiomas, astrocytomas, metastases, and all tumors. We also investigated the relationship between scan positivity and the number of months the scan was performed after the onset of symptoms.

Brain-scanning techniques underwent progressive change at our institution over the 10-year period. Figure 1-1 shows one of the earliest brain scans performed at the Johns Hopkins Hospital. The scan is a lateral view obtained with a rectilinear scanner with a 3-in.-diam NaI(Tl) detector 24 hr after injection of <sup>131</sup>I-labeled serum albumin. The use of <sup>99m</sup>Tc-pertechnetate began in 1964. Initially, a 10-mCi dose was injected intravenously without perchlorate or atropine, and anterior, posterior, and two lateral scan views were obtained. Since 1966, atropine and potassium perchlorate have been added to the protocol and the dose has progressively increased to its current level of 15–20 mCi. Vertex views were obtained routinely after the mid-1960s. Use of the Anger camera began in 1967 and has progressively increased (Fig. 1-2) until at this time the camera and scanner are used with about equal frequency. More recently, computer analysis has been added (1), and in many cases cerebral circula-



Fig. 1-1. One of earliest brain scans at Johns Hopkins Medical Institutions performed with rectilinear scanner with 3-in.-diam NaI(TI) crystal after injection of <sup>131</sup>Ilabeled serum albumin.

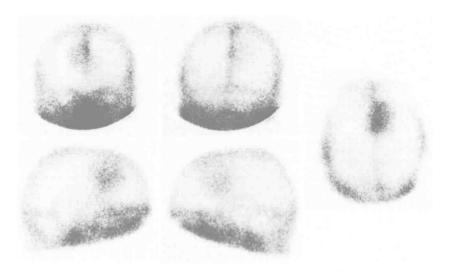


Fig. 1-2. Routine five-view brain scan of patient with meningioma performed with Anger camera and 15 mCi 99mTc-pertechnetate.

tion is evaluated from serial camera images obtained 2 sec apart after intravenous injection of the tracer as bolus (2) (Fig. 1-3).

#### Results

Frequency of studies. The number of brain scans increased by nearly a factor of 10 over the decade 1962-1972 (Fig. 1-4). From 1965 on, the number of arteriograms increased parallel with the number of scans, although the latter was about three times more numerous. By contrast, the number of air studies appeared to decrease slightly.

Relative accuracy. As shown in Fig. 1-5, the percentage of true positive brain scans did not change significantly over the 10-year period, remaining about 77% for all tumor types despite improvements in scanning techniques. Our accuracy level of 77% is somewhat lower than those of other reported series (3-5), which range between 82% and 84%, and equal to that reported by Wang, et al (6). The reasons for these differences are unknown.

Table 1-1 summarizes the number and percentage of positive pertechnetate scans and compares these to results of cerebral angiography, electroencephalography (EEG), and air studies (Air) for tumor type. For EEG, a positive result was indicated by the presence of an electrical abnormality in the hemisphere where the tumor was located, while positive results for all other studies refer to precise tumor localization.

The overall accuracy of air contrast studies (89%) exceeded that

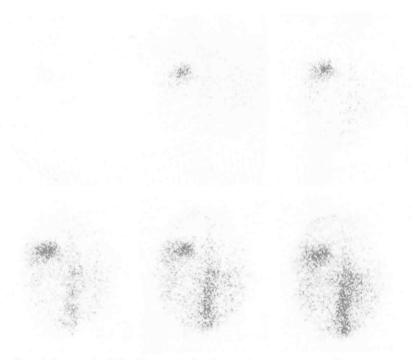


Fig. 1-3. Cerebral bloodflow study of patient with arteriovenous malformation.

of arteriography (84%), brain scanning (77%), and EEG (66%). However, air contrast studies were generally performed for the delineation of tumors in regions of the brain that are notoriously difficult to study by arteriography and brain scanning. The high detection rate by air studies of tumors near the posterior fossa and brain stem probably contributes significantly to the overall high percentage of positive air studies.

Accuracy as a function of location. Table 1-2 summarizes the accuracy of scanning, angiography, and air studies in relation to location of the tumor. Frontal tumors were detected more frequently by arteriography (82%) than by scans (77%) or air studies (70%). Parasagittal tumors were detected with greater than 93% accuracy by all three types of studies. Arteriograms detected 100% of temporal tumors, compared to 83% for air studies and 81% for scans. There was little difference in detection rate of parietal tumors (89–94%) among the three types of studies. Scans and arteriograms were similarly effective (90% and 86%) for detection of occipital tumors. There were no air studies in this group. Thalamic, sellar, and parasellar tumors were more accurately detected by air studies (92%) than by arteriograms (84%) or scans (60%). Both scans and arteriograms de-

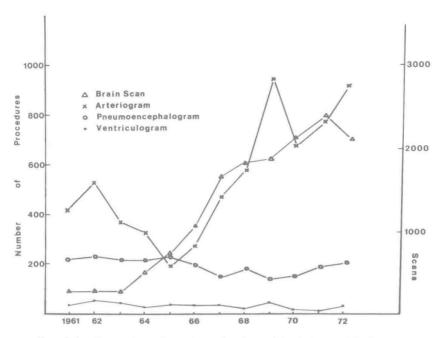


Fig. 1-4. Comparison of numbers of radiographic studies and brain scans performed.

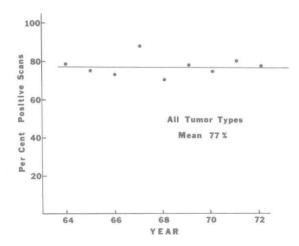


Fig. 1-5. Percentage of positive scans in all tumor types over the decade.

tected 100% of sphenoid wing meningiomas. These were not studied with air contrast procedures. Pontine tumors were most effectively detected by air studies and arteriography (78% and 80%), and least often by scanning (25%), the lowest scanning detection rate for any

Ten Years of Brain Scanning | 7