# MICHEL TER-POGOSSIAN AND THE DEVELOPMENT OF POSITRON EMISSION TOMOGRAPHY (PET)

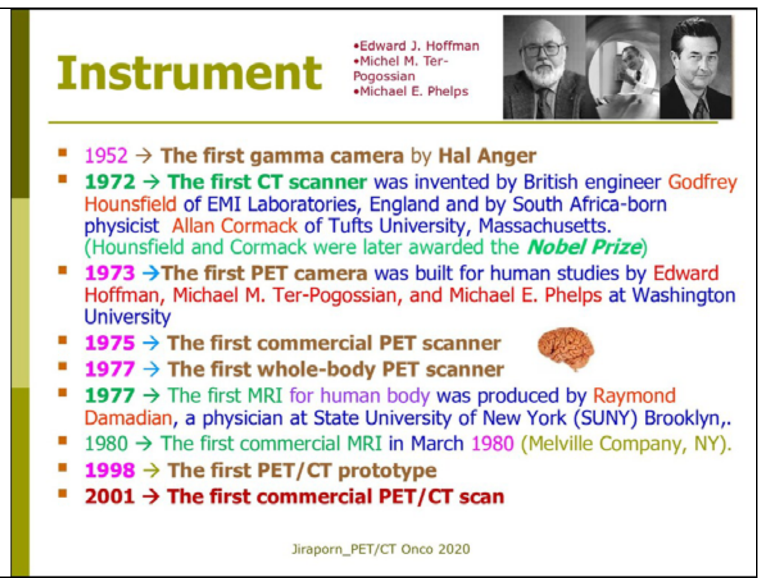
L. Rothenberg [1], P. Sprawls[2]

[1] Memorial Sloan Kettering Cancer Center, New York
[2] Emory University, Atlanta, and Sprawls Educational Foundation, www.sprawls.org

## I. INTRODUCTION

Although the development of most medical imaging methods and technologies is the result of contributions by a team of physicists, engineers, and physicians, there is often one individual whose vision, research, and leadership are a major factor resulting in the innovations and new imaging modalities. Physicist Michel Ter-Pogossian is one of those. Included in his extensive career was the recognition of the value and promotion of short-life radionuclides, especially oxygen-15, a positron emitter, for both research and clinical diagnostic procedures. This required the development and installation of cyclotrons within the clinic and methods for measuring radioactive uptake and decay in specific organs. Imaging the radiation from positron-emitting radionuclides with technology available at that time was a challenge because the high energy (511 keV) annihilation radiation was beyond the effective range of collimators. This ultimately led to imaging methods using time-of flight and co-instance localization and the development of positron emission tomography (PET. This resulted from the efforts of many medical imaging professionals, but for his major contributions Dr. Ter-Pogossian has been recognized as a "Father of PET".

Positron Emission Tomography (PET) is one of several computerized tomography imaging methods that are the foundations of modern clinical methods that have developed over the years.




PET is related to the other imaging modalities in several ways. The most significant was it provided visualization of conditions and functions within the human body not possible with the other methods. Although radionuclide imaging was well established with the gamma camera, including single-photon emission tomography (SPECT), the gamma camera using physical collimation to form images was not capable of effective imaging the higher-energy, 511 keV, annihilation photons produced by positrons. PET was developed using the reconstruction method first developed by Hounsfield and Cormack for CT. A major value of PET was being combined with CT to add biological function to the high-detail CT images.

## II. THE MANY ACHEIVMENTS AND CONTRIBUTIONS OF MICHEL TER-POGOSSIAN

Michel Ter-Pogossian was a pioneering medical physicist with many contributions throughout his career that are described in many publications, Reference (1, 2, 3,4). This article provides an overview of his life and career and his activities contributing to the development of positron emission tomography (PET).

*Early Life*

Michel Ter-Pogossian was born in Berlin, Germany on April 21, 1925, when his parents were in Germany due to an assignment that his father, a lawyer, was working as an envoy. Earlier his parents, who were Armeninan, had fled their homeland where there was ethnic persecution after World War I. Because of his family background he is frequently included in lists of famous Armenians or Famous Armenian Inventors.

When he was two months old, his family moved to Paris where Michel grew up and had his primary education. His fascination with science began as a child and was fueled by experiments involving his toy physics and chemistry kits. He attended the University of Paris and earned degrees in science from the University and from the Institute of Radium in 1943 and 1946, respectively. At the Institute of Radium, he studied under Irene Joliot-Curie. While a student he had a minor role in the French resistance and served as an advance scout when the French military was on the way back to Paris following the German retreat. He was in Paris when Charles DeGaulle arrived with the returning victorious Allied troops.

*Graduate Studies In the U.S.*

Ter-Pogossian moved to the United States to study at Washington University of St. Louis, where A. H. Compton, a physicist and Nobel laureate and a friend of his family, was the Chancellor of the university. There he received the M.S. degree in 1948 and a Ph.D. in Nuclear Physics in 1950.

*Academic Ranks*

Ter-Pogossian joined the Mallinckrodt Institute of Radiology at Washington University as an Instructor in Radiation Physics in 1950, and later held titles there of Professor of Radiation Physics in 1961, Professor of Biophysics in Physiology in 1964, and Professor of Radiation Sciences in 1973.

*Research Activities in St. Louis*

The physics department at Washington University had a cyclotron that had been used for atomic and nuclear research during World War II that was later converted to produce medically relevant isotopes such as 131-I and 32-P. There were efforts to produce the biologically relevant short-lived isotopes such as 11-C, 13-N, and 15-O, 18-F and a few patients were brought to that cyclotron and housed in a trailer next to the physics department for some early studies, but this probed to be an unacceptable situation. Also, the older cyclotron was designed to accelerate only deuterons. Ter-Pogossian was advised to approach the National Institutes of Health to obtain funding for a new cyclotron that would be located in the hospital complex at Washington University. He was successful in getting funding and a new cyclotron manufactured by Allis-Chalmers was obtained. With the use of the short-lived isotopes, He and his collaborators pioneered the use of radiotracers and developed practical clinical applications of cerebral scanning. His work resulted in improvements in medical imaging, external beam radiotherapy, and brachytherapy. Details of the research of Ter-Pogossian and his colleagues are given below.

Ter-Pogossian is often called the "Father of Positron Emission Tomography (PET)", although he sometimes preferred the title "Mother" since he worked with so many others to develop the early PET devices. Among those he cited as important contributors were his many colleagues at Washington University including Michael E. Phelps and Edward Hoffman, the invention of SPECT by David Kuhl and co-workers at the University of Pennsylvania, Gordon Brownell at Massachusetts General Hospital who developed the method to detect annihilation radiation from positrons, those at the Lawrence Berkely Lab who were able to produce the first medically useful radionuclides including 131I, 201Th, 99mTc, 14C, and 67Ga, James Robertson and colleagues at Brookhaven National Laboratory who built "headshirinker", a direct forerunner of PET, and Godfrey Hounsfield and Alan Cormack who developed the reconstruction algorithms which were used for PET, as well as for computed tomography.

*Important Interactions in England*

While working at Washington University, in the early days primarily as a radiation therapy physicist, Ter-Pogossian was able to take a six-month sabbatical where he studied with the noted physicist L.H. Gray on important animal experiments with short lived isotopes and he also visited Hammersmith Hospital in London which was operating a medical cyclotron.

*Publications and Editorial Boards*
Ter-Pogossian was a prolific author, with more than 250 papers and book chapters, and was a charter member of the American Nuclear Society and a fellow of the American Physical Society. He served on the editorial boards of major scientific journals, including the American Journal of Roentgenology, the Journal of Nuclear Medicine and the Journal de Biophysique & Medicine Nuclear. He also served as an adviser for several Department of Energy and National Institutes of Health committees.

*Popular Diagnostic Physics Textbook*
Michel Ter-Pogossian is well known to a certain generation of medical physicists for having published his outstanding textbook The Physical Aspects of Diagnostic Radiology, Hoeber Medical Division, Harper & Roe, Publishers, New York, Evanston and London, 1967. Surprisingly, there is no mention of nuclear medicine or radioactivity topics in the book. This book can be read and downloaded from the AAPM Author Archives at: DiagnosticRadiology.pdf (aapm.org)

*Personal Life and Family*
Michel Ter-Pogossian married Ann Scott (July 13, 1932 – April 17, 2022), who was the daughter of a major radiologist at Washington University, Dr. Wendell(?) 'Scottie" Scott. Ann was a widow with three children that Michel helped to bring up. She was an internationally known oil painter who exhibited her work initially as Ann Scott, but later as Ann Ter-Pogossian after they were married.
Michel Ter-Pogossian assumed emeritus status at Washington University in 1995. The following year while visiting Paris he died suddenly of a heart attack on June 19.

*Major Awards*
Michel Ter-Pogossian was honored by many organizations for his scientific endeavors including:
Paul E. Aebersold Award of the Society of Nuclear Medicine (now SNMMI) in 1976
Georg Charles de Hevesy Nuclear Medicine Pioneer Award of SNMMI 1985
Ter-Pogossian was elected the U.S. Institute of Medicine in 1987
Canada Gairdner International Award in 1993 (For Contributions to the development and application of Positron Emission Tomography)
Gold Medial Award of the Societe Francaise de Medecine Nucleare et de Biophysique

*Video Interview*
For those of you who would like to hear Michel Ter-Pogossian give a first-person description of his life and career, please visit the History and Heritage/Interviews section of the American Association of Physicists in Medicine website (aapm.org) to view a video interview lasting almost two hours conducted by Robert Gorson on May 24, 1993 at Washington University Medical Center in St. Louis. The link is: AAPM History and Heritage - Interviews

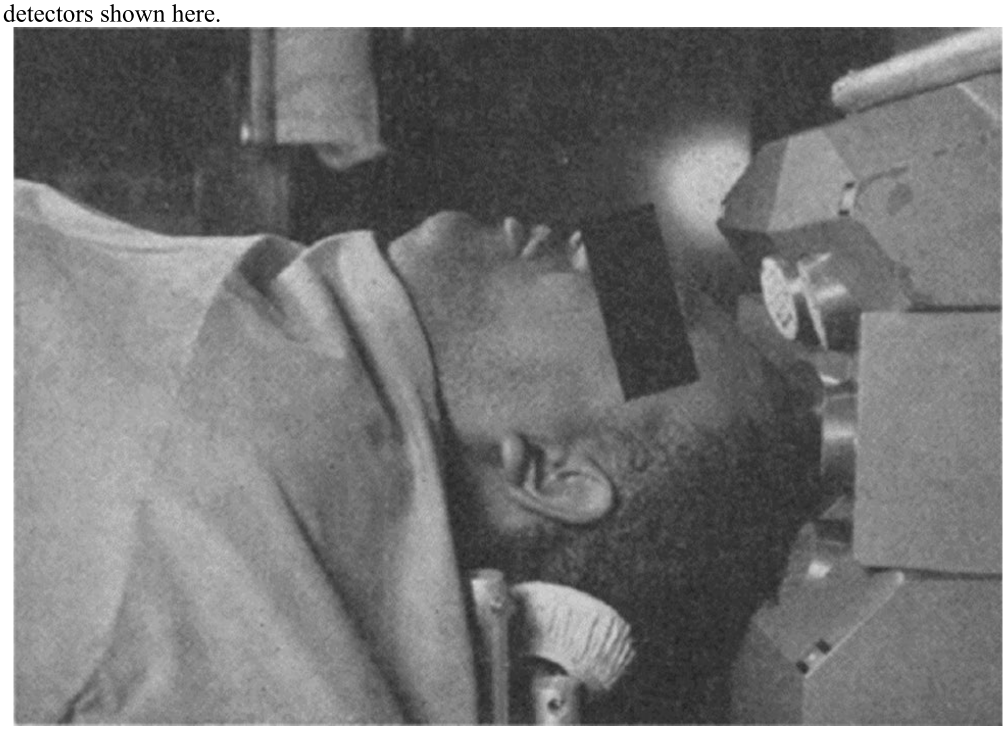
## III. THE DEVELOPMENT AND EVOLUTON OF POSITRON EMISSION TOMOGRAPHY (PET)

The development of positron emission tomography (PET), as described by Ter-Pogossian, took place through the combination of the following recognitions: (1) a handful of short-lived, positron-emitting radionuclides, carbon-11, nitrogen-13, and oxygen-15, exhibit chemical properties that render them particularly suitable for the tracing of important physiological pathways, and (2) the radiation emitted as a result of the annihilation of positrons in matter exhibited physical properties that made it well-suited for nuclear medicine imaging, particularly for tomographic reconstruction. The scientific building blocks that were necessary for the structure of PET were contributed over a period of several decades by many investigators in physics, mathematics, chemistry, and fundamental biology.

A comprehensive description of the development of positron emission tomography is provided by Ter-Pogossian in his article, *The Origins of Positron Emission Tomography*, and *A brief History of Positron Tomography* by Dayton A. Rich. These are included in the APPENDIX of this article where they can be read in detail. Much of the following is based on and contains excerpts from these articles article along with references to other publications by Ter-Pogossian.

## *IV.* THE VALUE OF SHORT LIFE RADIONUCLIDES

Generally, nuclear medicine imaging was limited to the use of radionuclides with relatively long half-lives because of technical limitations of producing, administering, and imaging before the nuclide decayed below a measurable level. Also, the lifetime of the radionuclide needed to be sufficiently long in relationship to dynamic physiology functions to provide for their measurement. For example, $^{15}O$ was thought to be clinically useless because of a short half-life (122.5 s) making it biologically insignificant. However, Ter-Pogossian in collaboration with others, used and demonstrated its value in several physiological studies, Reference (5) . $^{15}O$ was used as $^{15}O–O^{2}$, $^{15}O–CO$, and $^{15}O–CO^{2}$, for respiratory.
and cerebral metabolic studies. diseases. In a study, a small volume of blood with radioactive $^{15}O$ labeled hemoglobin ($^{15}O$-Hb) was rapidly injected into the
internal carotid artery of a patient. The buildup and decay of activity in the brain was measured with a configuration of six scintillation detectors shown here.

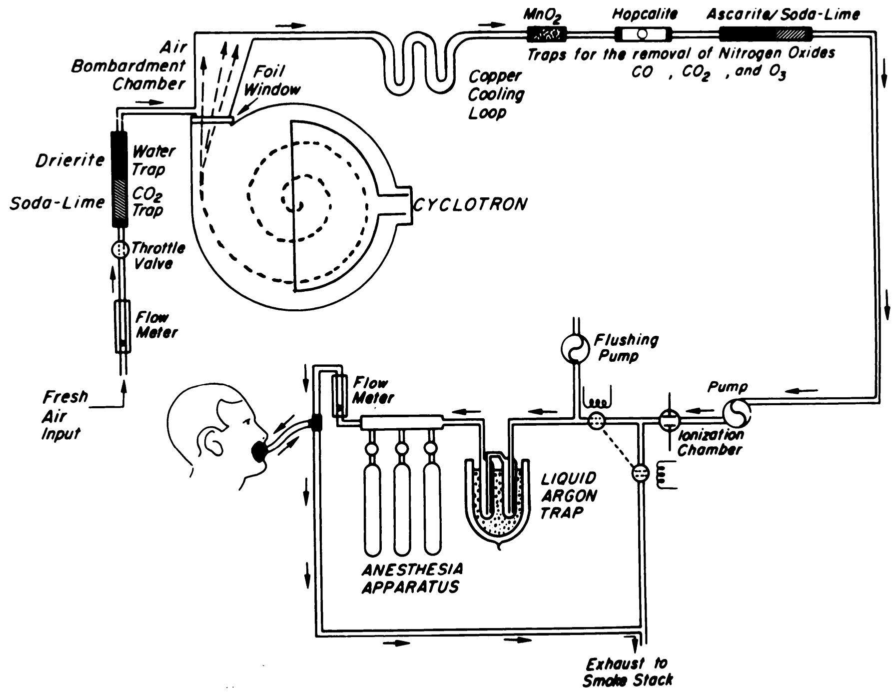


His analysis of the data provided a measurement of fractional oxygen utilization in the brain and regional cerebral oxygen utilization rates, Reference (6).

## *V. CYCLOTRONS TO PRODUCE SHORT LIFE RADIONUCLIDES IN THE CLINIC*

The positron-emitting radionuclides, carbon-11, nitrogen-13, and oxygen-15 are produced with proton bombardment in cyclotrons. At that time, cyclotrons were well developed and used in many institutions and organizations around the world. What was needed to produce the medically useful position emitting radionuclides were relatively small cyclotrons located in the clinic, not other departments some distance away. MT visited several cyclotron producers and installations, including in Japan and England, to learn more about their characteristics and capabilities.

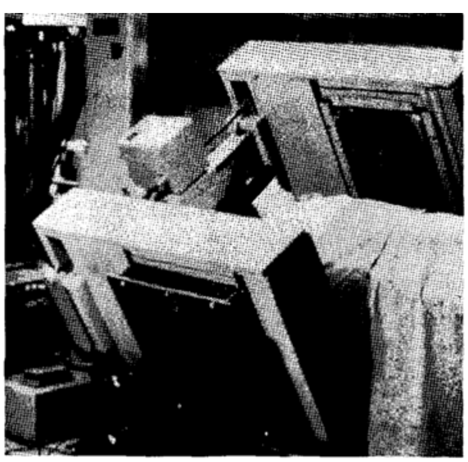
The decision was to install a cyclotron at the Washington University Medical Center manufactured by the Allis-Chalmers Company but by specifications developed by Ter-Pogossian and colleagues. This diagram shows the system used to deliver purified radioactive oxygen to a patient to evaluate respiratory function.




A full description of the characteristics and use of cyclotrons for producing radionuclides for imaging is described by Ter-Pogossian in Reference (7).

## VI. IMAGING SHORT LIFE RADIONUCLIDES

Initially, gamma cameras were used to image radiation from the short-life radionuclides in clinical procedures, including tomographic imaging. That was the technology available at the time. However, it was limited because the collimators were not efficient for the 511 keV photon annihilation radiation emitted by the positrons.



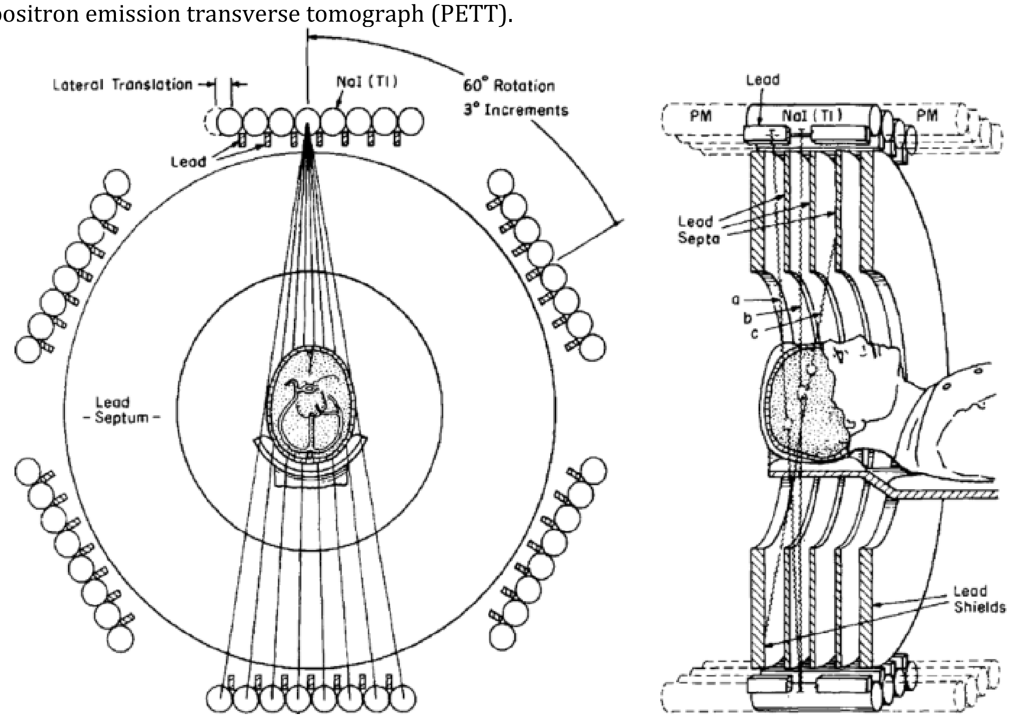
**The Massachusetts General Hospital positron camera. (Reprinted courtesy of Gordon L. Brownell and the Physics Research Laboratory at Massachusetts General Hospital.)**

## VII. POSITRON EMISSION TOMOGRAPHY (PET)

As Ter-Pogossian reported, It became apparent that for tomographic imaging, the annihilation radiation exhibited three major advantages over gamma rays: (1) the coincidence collimation of the annihilation radiation is a more efficient process than the collimation by absorption of gamma rays, (2) the coincidence detection of the annihilation photons allows a very accurate compensation for the attenuation of the radiation in tissues, and (3) the iso-response curves for the coincidence detection of annihilation photons are nearly uniform. This was to establish the principles of positron emission tomography.

In the early 1960s, Rankowitz et al. developed a positron scanner which consisted of scintillation detectors designed for coincidence detection, which simultaneously detects two 511 keV photons emitted at 180° through the annihilation reaction of electrons and positrons. Their report, *A Positron Scanner for Locating Brain Tumors* is included in the Appendix of this article.

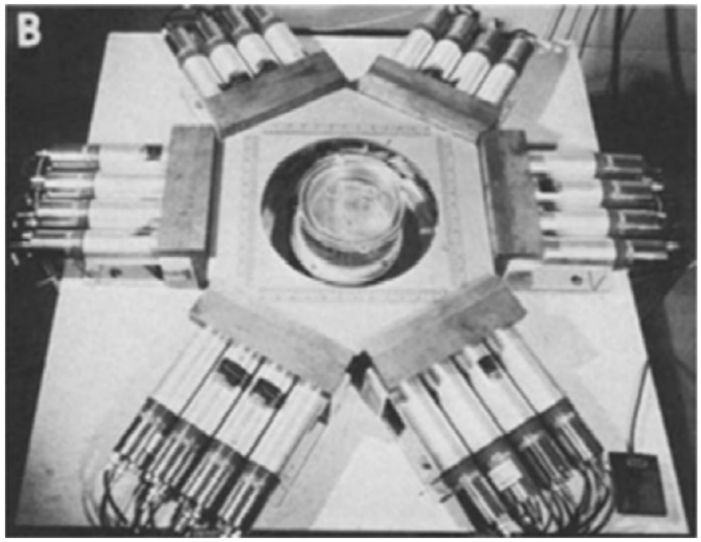
In the early 1970s, Ter-Pogossian's team developed a hexagonal system aiming for clinical human studies, which they named as positron emission transverse tomograph (PETT).




A major feature of the system was the development of fast electronics that were used for precise time-of-flight measurements that could identify and record the two annihilation photons from a specific positron interaction. This was used to determine the location of the position along a line between two detectors. By combining the positions along several lines between pairs of detectors, images could be reconstructed showing the distribution of the positions within a slice of tissue.

*This is the fundamental principle of positron Emission tomography (PET).*

Some of the initial development was conducted in the laboratory with a prototype using phantoms.




With the development of a system to produce tomographic images of the distribution of positron-emitting short-life radionuclides as shown here, the work continued to create the technology and methods for an expanding range of clinical applications, including whole body imaging and combined imaging with CT. One of the developments contributing to the future systems was the ring configuration of detectors that Dr. Ter-Pogossian is demonstrating here.

## REFERENCES

1. Focal Spot, (vol 27, no 2, 1996 (Published by the Mallinckrodt Institute of Radiology

2. Michel Ter-Pogossian | Encyclopedia MDPI. Link Michel Ter-Pogossian | Encyclopedia MDPI

3. Iwao Kanno1 · Miwako Takahashi1 · Taiga Yamaya1, Michel M. Ter-Pogossian (1925–1996): a pioneer of positron emission tomography weighted in fast imaging and Oxygen-15 applicationRadiological Physics and Technology (2020) 13:1–5; Published online: 11 December 2019 © Japanese Society of Radiological Technology and Japan Society of Medical Physics 2019

4. Michel M. Ter-Pogossian, 71; Led Research on PET Scanner; https://www.nytimes.com/1996/06/21/us/michel-m-ter-pogossian-71-led-research-on-pet-

5. Ter-Pogossian MM, Powers W.E. The use of radioactive Oxygen-15 in the determination of oxygen content in malignant neoplasm. Radioisotopes in scientific research. In: Proceedings of the 1st UNESCO international conference, vol 3. Paris 1957. New York: Pergamon; 1958.

6. Ter-Pogossian MM, Eichling JO, Davis DO, Welch MJ. The measure in vivo of regional cerebral oxygen utilization by means of oxyhemoglobin labeled with radioactive Oxygen-15. J Clin Invest. 1970;49:381–91.

7. Ter-Pogossian MM. Cyclotron produced short-lived radioactive isotopes. Am J Roentgenol Radium Ther Nucl Med. 1966;96:737–43. Presented at 47th Annual Meeting of the American Radium Society, **New** Orleans, Louisiana, April 8-10, 1965.

## APPENDIX

### Author Information

Lawrence N. Rothenberg, Ph.D. is Attending Physicist Emeritus in the Department of Medical Physics at Memorial Sloan Kettering Cancer where he is Director of the Medical Imaging Physics residency program. His main areas of interest in diagnostic radiology have included mammography, computed tomography, and education of radiology residents, medical physics students, and technologists. He is Past President of AAPM, Quimby Lifetime Achievement Awardee, Fellow of AAPM, ACR, ACMP, and HPS, and Distinguished Emeritus Member of NCRP.

Dr. Perry Sprawls

Perry Sprawls, Ph.D., is a clinical medical physicist and educator with a major interest in the preservation of the history and heritage of medical physics and related medical applications. Links to his other historical publications are on the website. www.sprawls.org Contact: sprawls@emory.edu

Contacts of the corresponding author:

Author: Lawrence N. Rothenberg, Ph.D
rothenbl@mskcc.org